The Indianapolis Asthma Study

Health Effects of Ozone and Other Environmental Measures on Children in the Indianapolis Metropolitan Area

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Hendricks Community	Danville
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Major	Shelbyville
Methodist	Indianapolis
Morgan County Memorial	Martinsville
Riley Children's	Indianapolis
Riverview	Noblesville
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1. INTRODUCTION

Asthma is one of the most common chronic conditions that affect Americans, especially children, and in the past two decades, the rate and number of asthmatic cases has grown at a dramatic pace. The estimated number of asthmatics in the United States more than doubled from 6.7 million in 1980 to 17.3 million in 1998 (CDC 1999). Asthma affects people of all ages, color, geographic location, and socioeconomic status. In the general population, the poor are at greater risk, and females are more likely than males to have asthma (NIH NHLBI 1999).

Deaths from asthma have been increasing for all age groups. Between 1979 and 1998, the age-adjusted mortality rate for asthma increased 55.6 percent.[1,2] There were 2,598 deaths from asthma in 1979 compared to 5,438 deaths in 1998. During this same period, however, the age-adjusted death rate attributed to all causes of death decreased 18 percent. In the general population, females and blacks are more likely to die from asthma than males and whites. (American Lung Association 2001)

Children are especially vulnerable to asthma, and the rate of asthma in children has been increasing more than for adults. In 1999, the Centers for Disease Control (CDC) reported that there were about 4.8 million children with asthma (CDC 1999). In children ages 5-14, the prevalence of asthma increased 74 percent from 1980 to 1993-1994 (from 42.8 per 1,000 to 74.4, respectively)[3] (NIH NHLBI 1999). Among children up to four years of age, the prevalence of asthma increased 160 percent from 1980 to 1993-1994 (from 22.2 per 1,000 to 57.8 per 1,000, respectively) (NIH NHLBI 1999). Poor children are at greater risk, and among children, unlike adults, boys (males) are more likely to have asthma than girls (females) (NIH NHLBI 1999).

[1] from 0.9 per 100,000 in 1979 to 1.4 per 100,000 in 1998.

[2] The number and rate of asthma deaths before and after 1979 are not directly comparable because of changes in the International Classification of Diseases codes. However, the increases in mortality attributed to asthma have been consistent through changes in the code over time.

[3] More recent data from the National Health Interview Survey (NHIS) estimated the prevalence of asthma in 1998 to be 53 per 1,000 population in the age group 0 to 17 years. The NHIS is a household interview survey of the civilian, noninstitutionalized population nationwide. The 1998 NHIS estimate measures asthma attack prevalence and produces lower estimates than data before 1997 when the National Health Interview Survey (NHIS) was redesigned. The lower estimates are produced because asthma attack prevalence requires a medical diagnosis of asthma and an episode or attack of asthma in the past twelve months to classify a person as having active asthma. This means that people who have asthma that is under control are not included in these estimates. Therefore, estimates using the NHIS data prior to 1997 cannot be compared to those after 1997. The 2001 NHIS will begin counting persons with well-controlled asthma. (National Center for Health Statistics 2001).

Asthma results in extensive utilization of health care in the form of outpatient visits to doctors' offices and hospital outpatient departments, visits to hospital emergency departments, and hospitalizations. In 1998 in the general population, asthma accounted for 13.9 million outpatient visits to private physician offices and hospital clinics, 2.0 million visits to emergency departments, and 423,000 hospitalizations. Blacks utilize these forms of health care more than whites, and females more than males. Asthmatic children utilize health care services extensively and at a higher rate than do asthmatic adults for outpatient visits, [4] emergency department visits,[5] and hospitalizations.[6] The highest utilization rates for these services occur among the youngest children (in the 0-4 year old age group). Children aged 0-17 had 5.8 million outpatient visits, over 867,000 emergency department visits, and over 89,000 hospitalizations in 1998. (National Center for Health Statistics, 2001)

Asthma affects the quality of life among all ages of and children and adults. It is believed to be the most common reason that children miss school (CDC 1999; PEW 2000) and this absenteeism, in turn, causes parents to lose time at work. Asthma accounts for an estimated three million lost work days for adults and 10.1 million lost school days for children annually (American Lung Association 2001). Nationwide, the direct and indirect health care costs for asthma have been estimated to be $11.3 billion in 1998 (NIH NHLBI 1999), and asthma-related costs for the year 2000 were estimated to exceed $14.5 billion (CDC 1999).

In Indiana, the estimated self-reported asthma prevalence is estimated to be 6.7 percent of the general population (NIH NHLBI 1999). During the period 1990-1995, blacks in Indiana experienced a death rate of 29.8 per 1,000 population for asthma as the underlying cause compared to a death rate of 14.4 per 1,000 for whites (Mannino and others 1998). In 1996, the Bowen Research Center's Community Health Assessment identified asthma as the number one cause of avoidable hospital admissions for children under 18 years of age in Marion County (Bowen Research Center 1996).

[4] Among children aged 0-17 years, the outpatient visit rate was 823 per 100,000 compared to a visit rate of 407 per 100,000 for adults 18 years and over.
[5] Among children aged 0-17 years, the emergency department visit rate was 124 per 10,000 compared to a visit rate of 59 per 10,000 for adults 18 years and over. The visit rate for children aged 0-4 years was 170 per 10,000.
[6] Among children aged 0-17 years, the hospitalization rate was 25 per 10,000 compared to a hospitalization rate of 13 per 10,000 for adults 18 years and over. The hospitalization rate for children aged 0-4 years was 47 per 10,000.

According to the Pew Environmental Health Commission (Pew 2000), asthma rates will continue to increase in the next decades. By the end of this decade, the Commission estimates that 1 in 14 Americans and 1 in 5 families will be afflicted with asthma if no action is taken to reverse the alarming increase in asthma rates. By 2020, these rates of increase will mean that the number of Americans with asthma will exceed the projected population of the states of New York and New Jersey combined. By 2020, the Commission projects similar alarming increases in the numbers of asthma-related deaths, a doubling in Medicaid and Medicare dollars spent on asthma health care, and direct and indirect asthma costs that total $18 billion. (Pew 2000)

At the present time, asthma cannot be cured, but it can be controlled through proper diagnosis, treatment, and the elimination of triggering events, such as exposure to increased levels of pollution and other environmental stressors. The effective control of asthma in children requires a partnership among parents, health care providers, environmental regulatory agencies, state and local health departments, and educators. The causes of asthma development are not known, but the research literature suggests that environmental and social conditions together play a key role in increasing the severity of the disease. Conducting research to increase understanding of asthma, therefore, is an important aspect of efforts to prevent and control asthma.

The Indianapolis Asthma Study has the following objectives:

- to develop a database and methodology for evaluating the relationship between asthma in children and their exposure to ozone air pollution;
- to evaluate the role of competing explanations, including other air quality measures, environmental conditions, and social conditions (age, race/ethnicity, income, and sex) on asthma in children residing in the Indianapolis metropolitan area; and
- to examine the effects of these conditions on other respiratory diseases.

The completion of the research described in this report will provide policymakers in central Indiana with information about one of the potential environmental triggers for asthma, ozone and other air pollution, along with social characteristics that affect admissions of children to hospitals in the central Indiana area. This research will assist policymakers in their efforts to target limited resources and education efforts to reduce the occurrence of asthma among children.

2. BACKGROUND: CHILDHOOD ASTHMA

Section 2 provides an overview of asthma signs, symptoms, and risk factors; summarizes the research literature on the role of outdoor air pollutants as they relate to childhood asthma; and discusses the issues associated with the use of hospital admissions data in the study of asthma. Finally, this section discusses the research hypotheses to be tested that were derived from the literature review.

2.1 Asthma Signs, Symptoms, and Risk Factors

Asthma is a chronic inflammatory disorder that is characterized by recurrent attacks of respiratory symptoms including wheezing, breathlessness, chest-tightness, and coughing, particularly at night and in the early morning. The model for the mechanisms underlying asthma begins with environmental risk factors, which are discussed below, that stimulate airway inflammation. Regardless of the level of asthma severity, some degree of airway inflammation is always present. The symptoms of asthma are caused by changes in the airways, bronchoconstriction, airway edema, chronic mucus plug formation, and airway remodeling that produce variable airflow obstruction, which is often reversible with or without treatment. Another component of the disease is that the airways become hyper responsive to a variety of stimuli (environmental factors). Over time, a patient's asthma will change depending on environmental factors, the patient's activities, management practices, and other factors. (NIH NHLBI 1997)

Asthma is a multi-factorial disease, which means there are many factors that cause and exacerbate it (NIH NHLIB 1997; Clark and others 1999). Based on current knowledge, it is likely that both genetic background and environmental factors play a role in its development. Scientific studies have demonstrated a strong link between environmental factors and asthma development and exacerbation, and there are many triggers that can provoke or precipitate an inflammatory response and airflow obstruction, or asthmatic attack. These factors include exposure to allergens such as pollen, dust, animal excretions (dander, urine, feces, and saliva), house dust mites, cockroaches, molds, and some foods; exposure to indoor air pollutants such as tobacco smoke and odors; exposure to outdoor air pollutants such as ozone, smog, sulfur dioxide, and nitrogen dioxide; cold weather; exercise; diet; and stress. Colds, rhinitis, sinusitis, and lung infections, such as bronchitis, have also been shown to be linked to asthma episodes (NIH NHLIB 1997; Clark and others 1999). It is clear that there are many conditions that can cause or exacerbate asthma, but the Indianapolis Asthma Study focuses on the outdoor air pollutants that may be associated with asthma.

2.2 Ozone and Other Air Pollutants as Risk Factors

Understanding the role of outdoor air pollution on asthma is complicated because the outdoor air environment is a complex mixture of natural and anthropogenic pollutants. Although air pollution is monitored extensively in the United States, the number and location of monitoring sites and pollutants monitored often are not comprehensive enough to characterize the variability in air quality at local and regional levels to facilitate epidemiologic studies of asthma. Further efforts are needed to characterize exposures to air pollutants, especially to hazardous air pollutants and mobile source emissions. A related issue that complicates one's understanding is that there is relatively little information on total exposures to individual pollutants. In the United States, adults and children spend more time indoors (at home, school, or work) than outdoors, and ozone and other pollutants can also be generated indoors by many different sources. Additionally, ozone and other outdoor pollutants can infiltrate, by passive or mechanical means, to the indoor environment, but there is comparatively less data on indoor exposures to ozone and other pollutants than for outdoor exposures.

Since the 1980s, there have been hundreds of scientific studies to evaluate the role that specific air pollutants, singly or in combination, play in the causation and exacerbation of respiratory disease. These studies have included human exposure studies in which human subjects are exposed to controlled concentrations of single or multiple air pollutants; field studies of lung function performance; and epidemiologic studies of population experiences based on hospital admissions, emergency room visits, and other health records.

Human exposure studies have demonstrated that ozone produces three types of response in human lungs. Ozone exposure causes irritative cough and substantial pain on inspiration, decrements in forced vital capacity (FVC) and forced expiratory volume (FEV1), and neutrophilic inflammation of the airway submucosa accompanied by biochemical changes (American Thoracic Society 1996). Field studies have also produced evidence that spirometric decrements are related to ozone exposure in "naturally" exposed children and adults engaging in outdoor activities (American Thoracic Society, 1996). Some studies have shown that symptoms and medication use also increase with exposure to air pollution in general, and ozone appears to be a key pollutant in these field studies (American Thoracic Society 1996). The relationship between asthma and other pollutants (in children and adults) and medical treatment has also been studied in epidemiologic field studies (in which patients are examined and/or tested) and in studies that utilize administrative records of admission to hospitals, emergency rooms, or home visits by physicians. The results of these studies for children and adults have been mixed. Some studies have demonstrated that ozone and other pollutants are important, but others have not (Balmes 1993; American Thoracic Society 1996).

The findings of key epidemiologic studies, which investigated the relationship between air pollution and children's health care based primarily on administrative records, are summarized in Section 2.2.1. A detailed summary of the environmental measures that were investigated is found in Appendix A (Table A.1), and Table A.2 provides a detailed summary of the findings from these studies. When the investigations in these studies included adults, the results are provided for the corresponding age groups. Strict comparisons of these studies are difficult because of variations in measurement methods, statistical analysis methods, age group definitions, periods of study, and different outcome measures. Nevertheless, the following sections summarize general, age-specific findings and patterns derived from this literature review and provide summary information on the environmental measures.

2.2.1 Studies Showing the Effect of Ozone on Respiratory Health in Children

2.2.2 Studies Showing a Positive Statistically Significant Effect for Ozone

Of the 25 studies of emergency room visits, hospital admissions, and house calls included in the literature review, 12 studies reported a statistically significant positive relationship between ozone concentrations and respiratory health in children. Eleven studies done in Helsinki, Ontario, Atlanta, Mexico City, London, Paris, and Singapore demonstrated that children sought more medical treatment for asthma as ozone levels increased (Pönkä 1991; Burnett and others 1994; White and others 1994; Romieu and others 1995; Buchdahl and others 1996; Pönkä and Virtanen 1996; Medina and others 1997; Anderson and others 1998; Chew and others 1999; Fauroux and others 2000; Tolbert and others 2000). One study demonstrated this relationship between ozone and other respiratory conditions in Vancouver (Bates and others 1990).

It is difficult to make comparisons of the ozone concentrations in these studies because of the differences in averaging times and times of year when the studies were conducted. The studies can be roughly grouped, however, using a guide of 0.12 ppm (235 µg/m^3) for maximum 1-hour averages and 0.08 ppm (157 µg/m^3) for maximum 8-hour average. These values correspond to the United States Environmental Protection Agency's (EPA) ozone standards (the wording of the averaging times for the standards is somewhat different, however). On this basis, the studies by Fauroux and others (2000) and Anderson and others (1998) have ozone concentrations clearly below the comparison concentrations. It also appears that the ozone concentrations in the studies by Pönkä (1991) and Pönkä and Virtanen (1996) fall below the guidelines, but strict comparisons are not possible because of differences in averaging times. The studies by Medina and others (1997), Chew and others (1999), Tolbert and others (2000), White and others (1994), and Romieu and others (1995) are clearly at or above the level of the comparison concentrations. Because of the differences in averaging times, the remaining three studies (Bates and others 1990, Buchdahl and others 1996, and Burnett and others 1994) are more difficult to classify based on these guidelines. In sum, 4 of the 12 studies showing a statistically significant effect for ozone and respiratory health had ozone concentrations that were below the numerical values of the EPA's standards, 5 of the studies had levels that were at or above the guidelines, and 3 studies could not be classified.

All but three of the studies (White and others 1994; Romieu and others 1995; and Fauroux and others 2000) were based on more than one year of data. In all of the studies, the pollutant concentrations were averaged in those instances when there was more than one monitoring site for a particular pollutant. None of the studies linked any of the pollutant concentrations to individual addresses, but the study by Burnett and others (1994) linked measurements to hospitals by region in Ontario. Pollutant lags of 0 to 3 days were important in studies showing a positive association for ozone and the outcome measures (emergency room visits for asthma, reactive airway disease, and acute wheezy episodes; hospital admissions for asthma; and asthma house calls by physicians). Only one of these studies (White and others 1994) reported using a study population that was predominantly indigent and black.

The summer season was analyzed in 5 of the 12 studies that demonstrated a statistically significant positive association for ozone and respiratory health, four for ozone and asthma (White and others 1994, Romieu and others 1995, Anderson and others 1998, and Tolbert and others 2000) and one for ozone and other respiratory conditions (Bates and others 1990).

Two of the 12 studies had mixed results for multivariate modeling -- that is, results were positive for ozone when variables were examined individually, but the association with ozone disappeared when other variables were included in the modeling (Chew and others 1999; Tolbert and others 2000).

Two of the 12 studies reporting a positive association between ozone and asthma are more problematic than the others. Pönkä and Virtanen (1996) report the ozone concentration was statistically significant for asthma (the treatment) and for digestive tract disorders (the control). The study by Burnett and others (1994) does not provide a clear-cut analysis for children because the subjects were split into two age groups (0-1 years and 2-34 years). The results were positive for ozone in both age groups, but the diagnosis of asthma is difficult in the 0-1 year old group and the 2-34 year old group includes adults.

In summary, of the 25 studies that were reviewed, 12 reported a positive association between ozone and treatment for asthma or other respiratory condition during all or part of the calendar year. Four of these studies reported a positive association for ozone and asthma during the summer months and one for ozone and other respiratory conditions during the summer months. Two of the 12 studies were problematic.

2.2.3 Studies Showing No Statistically Significant Effect for Ozone

There were 12 studies that did not demonstrate a statistically significant relationship between ozone exposure and medical treatment visits for asthma in children in Ontario, Vancouver, Melbourne, Hong Kong, Seattle, St. John (New Brunswick), Sydney, Mexico City, and London (Bates and Sizto 1983, 1987, Bates and others 1990, Rennick and Jarman 1992, Tseng and others 1992, Schwartz and others 1993, Burnett and others 1995, Stieb and others 1996, Sunyer and others 1997, Morgan and others 1998, Rosas and others 1998, Atkinson and others 1999). One of these studies was a meta analysis of data from Barcelona, Helsinki, Paris, and London (Sunyer and others 1997).

It is more difficult to make comparisons of the ozone concentrations in these studies than for studies that showed a positive association for ozone because of the relative lack of environmental data. Using the numerical values of the EPA's standards as a guide, there were 2 of 12 studies (Stieb and others 1996 and Atkinson and others 1999) that had ozone values greater than 0.12 ppm (235 $\mu g/m^3$) for maximum 1-hour averages or 0.08 ppm (157 $\mu g/m^3$) for maximum 8-hour averages. The study by Rosas and others (1998) could also be grouped as a study with high ozone concentrations. One study (Morgan and others 1998) had ozone concentrations that were clearly below the EPA comparison values. There were eight studies that could not be classified, either because there were insufficient data (Bates and Sizto 1987 and 1990, Burnett and others 1995, Sunyer and others 1997) or because no data were provided (Bates and Sizto 1983, Rennick and Jarman 1992, Tseng and others 1992, Swartz and others 1993). In sum, 1 of the 12 studies that did not demonstrate a statistically significant effect for ozone and respiratory health had ozone concentrations that were below the numerical values of the EPA's standards, 3 of the studies had levels that were at or above the guidelines, and 8 studies could not be classified.

All but two of the studies (Rennick and Jarman 1992; Rosas and others 1998) were based on more than one year of data. In all of the studies the pollutant concentrations were averaged in those instances when there was more than one monitoring site for a particular pollutant. None of the studies linked any of the pollutant concentrations to individual addresses, but the study by Burnett and others (1995) linked measurements to hospitals by region in Ontario. Pollutant lags of 0 to 4 days were used throughout the studies that showed a nonsignificant association between ozone and the outcome measure.

Ozone was not significant for asthma in five studies that included summer season data (Bates and Sizto 1983, 1987; Bates and others 1990; Stieb and others 1996; Rosas and others 1998). The 1983 and 1987 studies by Bates and Sizto provided a long-term look at southern Ontario and may be considered as one study. The seven remaining studies used the calendar year of data.

As a group, the adequacy of the environmental data is more difficult to evaluate in these studies because of a lack of specificity in reporting the methodologies used. The study by Tseng and others (1992) was not strictly comparable because it utilized quarterly mean concentrations of the pollutant parameters and the hospital admissions, and the study by Burnett and others (1995) provided only summary information on ozone.

2.2.4 Studies Showing a Negative Statistically Significant Effect for Ozone

Three studies reported negative statistically significant effects for ozone. Garty and others (1998) reported that visits for medical treatment by children in Israel decreased as the ozone concentration increased for an analysis that included a calendar year of data, but other pollutants demonstrated a positive result for medical treatment visits. Anderson and others (1998) reported that hospital admissions for children in London (5 calendar years of data) increased with decreasing ozone concentration in winter, but increased with increasing ozone concentrations in summer. Ozone was not significant during the analysis that included both summer and winter data. Holmén and others (1997) also reported a negative relationship between asthma emergency room visits and ozone concentrations for an analysis that included three calendar years of data in Halmstad, Sweden.

Using the numerical values of the EPA's standards as a guide for comparing the ozone concentrations in these studies, there were 2 of 3 studies (Anderson and others 1998 and Holmén and others 1997) that had ozone concentrations that were clearly below the EPA comparison values and the third study (Garty and others 1998) could not be classified because of differences in the averaging times reported.

The adequacy of the environmental data is difficult to compare in these studies. The environmental data in the study by Anderson and others (1998) included more monitoring sites than the other two studies (Garty and others 1998, Holmén and others 1997), and it included multiple years of data. The studies by Garty and others (1998) and Anderson and others (1998) used comparable monitoring methodologies.

2.2.5 Studies Showing the Effect of Air Quality Measures Other than Ozone on Respiratory Health in Children

The information is also mixed for other pollutants, meteorological variables, pollen, and mold; however, sulfur dioxide, nitrogen dioxide, and particulate matter emerge as three additional important air pollution variables. Eight of 21 studies that included sulfur dioxide demonstrated a positive and statistically significant relationship between medical treatment by children for sulfur dioxide and the outcomes measures. Seven of these studies were for sulfur dioxide and asthma (Romieu and others 1995, Buchdahl and others 1996, Medina and others 1997, Sunyer and others 1997, Atkinson and others 1999, Anderson and others 1998, Garty and others 1998, Chew and others 1999) and one study was for sulfur dioxide and other respiratory conditions in winter (Bates and others 1990). The sulfur dioxide relationship was negative in one study (Tseng and others 1992).

It is difficult to compare the sulfur dioxide concentrations in these studies because of differences in averaging times and lack of information. However, the study by Romieu and others (1995) had maximum 24-hour concentrations that were greater than the numerical value of the EPA 24-hour standard of 365 µg/m^3. The 24-hour maximum concentration was considerably less than the EPA 24-hour standard in other studies (Medina and others 1997, Anderson and others 1998, Atkinson and others 1999, Chew and others 1999). There was insufficient information to determine the 24-hour maximum concentrations in the studies by Buchdahl and others 1996, Sunyer and others 1997, Garty and others 1998, Bates and others 1990, and Tseng and others 1992.

Nine of 21 studies which included some measure of the oxides of nitrogen found a statistically significant positive relationship between medical treatment visits by children for asthma in children (Pönkä 1991; Medina and others 1997; Sunyer and others 1997; Morgan and others 1998; Atkinson and others 1999; Anderson and others 1998; Garty and others 1998; Holmén and others 1997; Chew and others 1999). The relationship was negative in winter in one of the studies (Bates and Sizto 1987) but not significant during the summer.

The concentrations of the oxides of nitrogen in these studies can be described as relatively low based on a comparison to the numerical value of the EPA's annual standard of 0.053 ppm (100 µg/m^3). The study by Garty and others 1998 had the highest levels of the oxides of nitrogen and these appeared to exceed 0.053 ppm based on visual examination of a graph of weekly data.

The reviewed studies included different measures of particulate matter (PM13, PM10, PM2.5, black smoke, coefficient of haze, visibility, API), which makes comparisons difficult. Seven of the 21 studies using particulate matter showed a positive and statistically significant association for asthma in children (Medina and others 1997; Rennick and Jarman 1992; Tseng and others 1992; Schwartz and others 1993; Atkinson and others 1999; Chew and others 1999; Tolbert and others 2000). There was a positive and statistically significant relationship for sulfate and asthma in three of four studies in which it was included (Burnett and others 1994, 1995; Bates and others 1990). The 1994 Burnett study is limited because of the age groupings for children (0-1 years and 2-34 years). Comparisons among the particulate and sulfate data are not possible because of differences in the measures and averaging times used.

Pollen was found to be significant for asthma in one of eight studies that included pollen (Rosas and others 1998) and carbon monoxide was important for other respiratory conditions in one of two studies that included carbon monoxide (Atkinson and others 1999)

Of the meteorological variables included in the studies which were reviewed, only temperature was included in enough studies to allow a summary of findings. The findings for temperature are difficult to interpret because a large proportion of the studies (6 of 16 studies) that included temperature in the age group 0-14 years did not provide enough information to discern the role of temperature. Three of the remaining 10 studies reported a positive association between the outcome measures and temperature (Tolbert and others 2000, Bates and Sizto 1987, Rosas and others 1998), two reported a negative association (Buchdahl and others 1996, Pönkä and Virtanen 1996), and five reported that temperature was not significant (Pönkä 1991, White and others 1994, Romieu and others 1995, Bates and Sizto 1987, Bates and others 1990). The article by Bates and Sizto (1987) appears in two categories because it reported seasonal effects. Overall, the reviewed literature is interpreted to support a positive association between temperature and the outcome measures based on the studies that showed a statistically significant association.

There were five studies that included relative humidity in the statistical analysis, and in four of these studies the relationship for relative humidity was not significant, and one of the studies did not provide enough information to discern the relationship.

2.2.6 Summary of Epidemiologic Studies Showing the Effect of Air Pollution on Respiratory Health in Children

When the epidemiologic studies are viewed collectively, several patterns emerge. Overall, the number of studies that reported a positive and statistically significant effect for ozone and asthma or other respiratory conditions (10-12 studies, depending on whether the two most problematic studies are included) was roughly equal to the number of studies that did not show a significant effect for ozone (10-12 studies, depending on whether the Bates and Sizto studies are counted separately or combined and whether the 1995 Burnett study is counted). Three studies reported a negative and statistically significant effect for ozone. When the studies are segregated according to the seasonal time period analyzed, the majority are positive for ozone during the summer season (5 out of 8 summer season studies, counting the Bates and Sizto studies of southern Ontario as one study). This finding suggests that ozone is related to health care for asthma and other respiratory conditions in children, and that an all-year analysis for ozone, which is formed during higher temperatures, may dilute the seasonal effect of the pollutant.

Other pollutants that appear to be important are sulfur dioxide, nitrogen dioxide, and particulate matter. A positive and statistically significant relationship was reported for sulfur dioxide and nitrogen dioxide in 9 of 21 studies involving these pollutants and in 7 of 21 studies involving particulate matter. Although the sulfate data are limited to only four studies, positive results in three of the studies suggest that it may be an important pollutant in relation to respiratory disease.

2.3 Research Hypotheses

The research hypotheses developed from the asthma literature that will be analyzed for the Indianapolis metropolitan area are:

- Admissions to hospitals for asthma and other respiratory diseases in children will increase as the concentration of ozone increases.
- Admissions to hospitals for asthma and other respiratory diseases in children will increase as the concentration of sulfur dioxide increases.
- Admissions to hospitals for asthma and other respiratory diseases in children will increase as the concentration of nitrogen dioxide increases.
- Admissions to hospitals for asthma and other respiratory diseases in children will increase as the temperature increases.
- Younger children are more likely than older children to be admitted to hospitals for asthma and other respiratory diseases.
- Non-white children are more likely than white children to be admitted to hospitals for asthma and other respiratory diseases.
- Children from lower income households are more likely than children from higher income households to be admitted to hospitals for asthma and other respiratory diseases.
- Boys are more likely than girls to be admitted to the hospital for asthma and other respiratory diseases.

2.4 Asthma Diagnoses and the Reliability of Hospital Data

There are quality issues related to the use of hospital and other health institution administrative records for epidemiologic studies of asthma and air pollution. To have a quality study, the diagnosis of asthma must be made correctly by the physician and the case must be correctly entered into a database. There is some evidence that this assumption may not always be supported in practice. The potential magnitude of the error and the reasons for the misclassification of asthma are not well documented, but some of the literature is summarized below.

The diagnosis of asthma in children must exclude other potential conditions that produce similar symptoms. These include allergic rhinitis and sinusitis, viral bronchiolitis, bronchitis, pneumonia, vocal cord dysfunction, vascular rings, laryngeotracheomalacia, tumor or enlarged lymph nodes, cystic fibrosis, bronchopulmonary dysplasia, and aspiration due to gastroesophageal reflux (Bieler 2000; NIH NHLBI 1997). In children less than one year of age, the distinctions between asthma, bronchiolitis, and asthma are especially difficult. The misclassification of the diagnosis for asthma has been identified as a potential problem for children with asthma (CDC 1999). The National Asthma Education and Prevention Program of the National Heart, Lung and Blood Institute (NIH NHLBI) of the National Institutes of Health (NIH) has issued guidelines developed by an expert panel that provide a means of interpreting symptoms and differentiating what is and what is not asthma (NIH NHLBI 1999). However, there is anecdotal evidence that primary health care providers may not be using these guidelines in sufficient numbers, resulting in misdiagnoses and children who go untreated (CDC 1999).

The reliability of hospital and health care service databases that are routinely used in epidemiologic studies has been questioned (U.S. EPA 1986; Bennett 1981). The EPA (1986) has commented on the use and limitations of hospital statistics in environmental studies, and it has stressed that the problems of misclassification may exist in the same or among different medical facilities. In responding to the EPA opinion, Bates and others (1990) have commented that the EPA did not recognize that misclassification can only weaken an association, and that the EPA did not provide data to show how the use of hospital data could lead to a false conclusion. The authors suggest that hospital emergency room visits can be used to provide useful information, provided that the study includes sufficient time and a sufficient number of institutions, separates effects by season, controls for differences between day of the week admissions or visits, and separates age groups.

Delfino and others (1993) evaluated the reliability of hospital data for population-based studies of air pollution by comparing reabstracts of 1,279 discharge records from 14 Montreal hospitals with the universal health insurance database of Quebec. The medical archivist, who reviewed each medical chart and discharge summary, was blinded to the database discharge diagnosis. The authors found agreement levels on discharge diagnoses of 94.9 percent for asthma. The agreement level for all other 3-digit ICD-9 respiratory codes was a relatively low 75.5 percent. However, when the groups were more broadly defined, the agreement increased to 90 percent for the respiratory comparison. The non-respiratory comparison group had an agreement level of 93.1 percent. In this study, the authors reported that diagnostic agreement varied from 59.3 percent to 94.9 percent across hospitals, and the disagreements were smaller in larger hospitals than in smaller ones.

Increasing the number of institutions can help ensure that a large enough number of cases will be available for the analysis. However, based on the authors' experience with the Indianapolis study, it is also clear that increasing the number of institutions also increases the potential for diagnostic misclassifications, and each hospital's coding methodology must be examined to ensure uniformity.

3. ENV. CONDITIONS - CENTRAL IN., '97-'99

Section 3 provides a summary of the environmental conditions present in central Indiana for the air quality and meteorological conditions that were included in the Indianapolis Asthma Study. The air quality conditions that existed during the study period are characterized in terms of comparisons to the National Ambient Air Quality Standards (NAAQS) established by the EPA, and to concentrations of pollutants within Indiana, to surrounding states, and to the nation.

The primary NAAQS (Table 3-1), which have been established to protect the public against adverse health effects, only address ambient exposures. These standards do not take into account potential exposures that can result from indoor sources. The NAAQS are revised as new knowledge is derived from exposure studies, including animal, human exposure, and epidemiologic investigations. Other pollutants may pose respiratory health hazards, but these pollutants are not well characterized in the ambient air and scientific studies of their role in the development and exacerbation of asthma are limited.

3.1 Air Quality Measurements

The Indiana Department of Environmental Management (IDEM) provided air quality data from its monitoring network, which it maintains in conjunction with local jurisdictions throughout the state. The monitoring network includes sites that are located in industrial, agricultural, commercial, and residential environments in rural, suburban, and urban settings. All of the data provided by IDEM, which are a part of the EPA's Aerometric Information Retrieval System (AIRS) database, are quality assured data. During the period of study (May 1 - September 30, 1997-1999), the central Indiana regional network included 9 ozone stations, 4 nitrogen dioxide stations, 9 sulfur dioxide stations, 17 particulate matter PM-10 stations, 4 lead stations, and 2 carbon monoxide stations.

Initially, the investigators had hoped to include all air quality pollutants measured by the network in the analysis. Some of the measures, however, were excluded from the analysis because they did not meet the screening criteria, which are identified below. The final data set for the study period included 9 ozone monitoring stations, 1 nitrogen dioxide station, and 4 sulfur dioxide stations. Appendix B provides a listing of stations and addresses for the final data set along with a summary of the completeness of the data at each monitoring station. Figure 3-1 shows the locations of the monitoring sites, and Table 3-2 provides summary data for the air quality variables over the period of study.

Table 3-1: National Ambient Air Quality Standards (NAAQS)

Pollutant	Standard Value		Standard Type
Carbon Monoxide (CO)			
8-hour Average	9 ppm	(10 mg/m^3)**	Primary[1]
1-hour Average	35 ppm	(40 mg/m^3)**	Primary
Nitrogen Dioxide (NO2)			
Annual Arithmetic Mean	0.053 ppm	(100 μg/m^3)**	Primary & Secondary[2]
Ozone (O3)			
1-hour Average[3]	0.12 ppm	(235 μg/m^3)**	Primary & Secondary
8-hour Average	0.08 ppm	(157 μg/m^3)**	Primary & Secondary
Lead (Pb)			
Quarterly Average		1.5 μg/m^3	Primary & Secondary
Particulate <10 micrometers (PM-10)			
Annual Arithmetic Mean		50 μg/m^3	Primary & Secondary
24-hour Average		150 μg/m^3	Primary & Secondary
Particulate <2.5 micrometers (PM-2.5)			
Annual Arithmetic Mean		15 μg/m^3	Primary & Secondary
24-hour Average		65 μg/m^3	Primary & Secondary
Sulfur Dioxide (SO2)			
Annual Arithmetic Mean	0.03 ppm	(80 μg/m^3)**	Primary
24-hour Average	0.14 ppm	(365 μg/m^3)**	Primary
3-hour Average	0.50 ppm	(1300 μg/m^3)**	Secondary
**Parenthetical value is an approximately equivalent concentration			
SOURCE: U.S. EPA. 2001a. "National Ambient Air Quality Standards (NAAQS)." Available at: http://www.epa.gov/air/oaqps/greenbk/criteria.html . Retrieved 2/02/2001.			
[1] Primary standards are established to protect the public from adverse health effects. [2] Secondary standards are established to protect against welfare effects such as damage to crops, buildings, ecosystems, and reduced visibility. [3] The ozone 1-hour standard applies only to areas that were designated nonattainment when the ozone 8-hour standard was adopted in July 1997. This provision allows a smooth, legal and practical transition to the 8-hour standard.			

3.1.1 Ozone

Ozone is a highly reactive, but not very soluble, gas that is produced in the atmosphere during the summertime months by sunlight-driven reactions involving volatile organic compounds (VOCs) from a variety of sources and nitrogen oxides (NOx), which are produced primarily by mobile and stationary combustion sources. Ozone is a common summertime pollutant in Indiana and other regions of the United States. The ozone monitoring network in the study area includes nine monitoring sites, which met the study's criteria for completeness. The monitoring locations are in Monrovia, Noblesville, Pendleton, Fortville, and Indianapolis. These monitors generate instantaneous ozone measurements that are reported as hourly averages and as 24-hour mean observations. The percent of missing data ranged from 0.2 percent at the Pendleton sites to 4.4 percent at the Fortville site.

In central Indiana, the ozone concentrations typically increase from the southwest to northeast, based on the pattern of prevailing winds and the input of precursor emissions to the air stream. The daily 24-hour mean and daily 1-hour maximum ozone levels averaged across all monitoring sites during the period of study were 0.038 ppm and 0.066 ppm, respectively (Table 3-3).

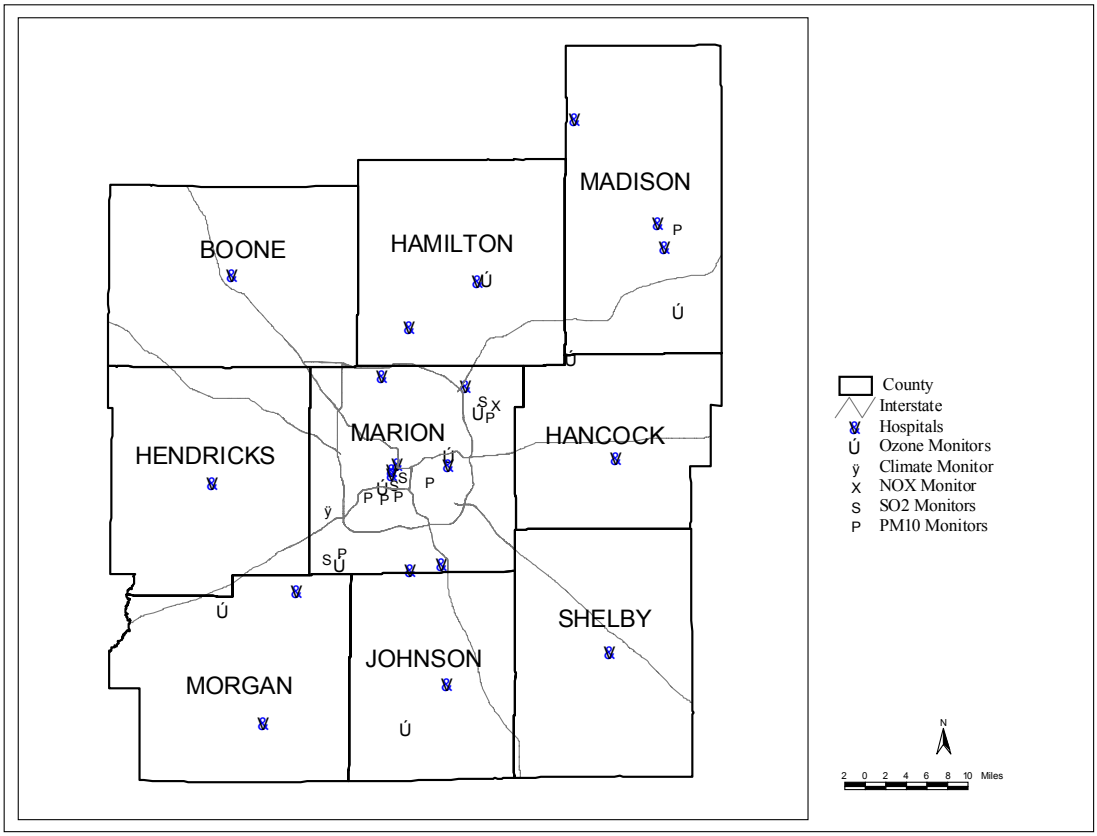

Figure 3-1: Location of Air Quality Monitoring Sites in the Indianapolis Metropolitan Area, 1997-1999

One picture of the ozone air quality in the study area can be obtained by comparing the measured levels to the primary National Ambient Air Quality Standard (NAAQS) for ozone. The NAAQS for ozone include a current 1-hour average and a revised 8-hour average concentration (U.S. EPA 1997; 2001a)[7]. The 1-hour standard is 0.12 ppm not to be exceeded more than once per year, based on data from a continuous monitor averaged over three consecutive years. This standard applies only to areas that were designated nonattainment when the ozone 8-hour standard was adopted in July 1997. The 8-hour standard is 0.08 ppm, and to attain this standard, the 3-year average of the 4th highest daily maximum 8-hour average of continuous ambient air monitoring data over each year must not exceed 0.08 ppm. The revised 8-hour standard was developed to provide greater protection to people who spend a significant amount of time working or playing outdoors—a group that is particularly vulnerable to the effects of ozone.

In the study area, the historical record of compliance with the 1-hour ozone standard shows that Marion County (City of Indianapolis) had been designated as a marginal area for compliance with the ozone standard during 1992-1994, but it was redesignated as an attainment area in 1994, and it has remained in compliance since then (U.S. EPA 2001b). Of the nine counties in the study area, six counties (Hamilton, Hancock, Johnson, Madison, Marion, and Morgan) exceeded the 8-hour ozone NAAQS of 0.08 ppm (U.S. EPA 2001c). In the Indianapolis Metropolitan Statistical Area, the trend in ozone concentrations since 1990 has been increasing for the 8-hour average, but it has not changed for the 1-hour average (U.S. EPA 2001d, 203).

[7] In a May 1999 split decision, the U.S. Court of Appeals for the D.C. Circuit limited the manner in which the EPA can implement the 8-hour standard. The Court of Appeals did not question the scientific basis for the new standard or the need for it. The EPA appealed this decision to the U.S. Supreme Court, which has agreed to hear the case. (U.S. EPA 2001a) .

Another picture of ozone air quality in the study region is provided by the EPA's Air Quality Standards Index (AQI)[8]. The AQI, which is reported only for large metropolitan areas, is an index for reporting air quality that focuses on health effects that can occur within a few hours or days within breathing polluted air. An AQI value over 100 is considered to be unhealthy, and it corresponds to 8-hour ozone concentrations greater than 0.08 ppm. Overall, the study area experienced good to moderate ozone air quality as defined by the EPA's AQI categories for ozone, but the region did have periods of elevated ozone when the ozone AQI values were greater than 100. There were twelve days in 1997 that had unhealthy ozone based on the EPA's Air Quality Index for ozone, nineteen days in 1998, and twenty-one days in 1999 (U.S. EPA 2001d, 221). In comparison to 94 other metropolitan statistical areas in the United States, Indianapolis' ranking worsened over the 3-year period, moving from 59th in 1997 to 61st in 1998 and to 68th in 1999 (a higher ranking indicates better air quality than a lower ranking).[9]

[8] The Pollutant Standards Index (PSI) was the predecessor to the AQI. The PSI was updated in 2000 and renamed the AQI. The two indices are similar, but the AQI includes a new health risk category, unhealthy for sensitive groups, and two additional pollutants - ozone averaged over 8 hours and fine particulate matter. Both the PSI and the AQI use an index value of 100 to represent pollutant concentration at the level of the NAAQS. (U.S. EPA 2001e)

[9] Based on data in Table A-18, pp. 221-222 in U.S. EPA 2001d.

Table 3-2: Summary Data for Air Quality Variables in the Central Indiana Study Area, 1997-1999[1]

Variable	No. Obs.	% Missing Data	Mean	SD	Percentile								
					Min	5th	10th	25th	50th	75th	90th	95th	Max
Ozone (ppm)													
daily mean	4048	2.0	0.038	0.011	0.008	0.020	0.023	0.030	0.037	0.045	0.054	0.058	0.078
daily 1-hour max	4094	0.9	0.066	0.018	0.002	0.037	0.043	0.053	0.065	0.077	0.089	0.096	0.135
2-day moving ave	4014	2.8	0.038	0.010	0.008	0.022	0.025	0.031	0.038	0.045	0.052	0.055	0.074
3-day moving ave	3978	3.7	0.038	0.009	0.011	0.023	0.026	0.032	0.038	0.044	0.050	0.053	0.071
Nitrogen Dioxide (ppm)													
daily mean	455	0.9	0.016	0.007	0.002	0.007	0.009	0.011	0.016	0.021	0.025	0.027	0.044
daily 1-hour max	459	0	0.037	0.014	0.005	0.015	0.019	0.028	0.037	0.047	0.055	0.060	0.095
2-day moving ave	452	1.5	0.016	0.006	0.003	0.008	0.009	0.012	0.016	0.020	0.024	0.029	0.040
3-day moving ave	449	2.2	0.016	0.005	0.004	0.009	0.010	0.013	0.016	0.020	0.023	0.025	0.038
Sulfur Dioxide (ppm)													
daily mean	459	0	0.005	0.003	0.001	0.002	0.002	0.003	0.004	0.007	0.009	0.011	0.018
daily 1-hour max	459	0	0.033	0.026	0.002	0.006	0.008	0.013	0.026	0.045	0.065	0.087	0.146
2-day moving ave	456	.7	0.005	0.002	0.001	0.002	0.002	0.003	0.005	0.006	0.008	0.009	0.013
3-day moving ave	453	1.3	0.005	0.002	0.002	0.002	0.003	0.003	0.005	0.006	0.008	0.009	0.011

[1]For the period May 1- September 30, 1997-1999.

Table 3-3: Summary of 2nd Highest Ozone 1-Hour Levels in Marion County, Adjacent States, and the United States

Area	Population[1]	2nd Highest Ozone 1-Hour Concentration (ppm)		
		1997	1998	1999
Boone County	38,147	—[2]	—	—
Hamilton County	108,936	0.114	0.125	0.114
Hancock County	45,527	0.109	0.119	0.104
Hendricks County	75,717	—	—	—
Johnson County	88,109	0.102	0.101	0.105
Madison County	130,669	0.091	0.117	0.105
Marion County	797,159	0.106	0.115	0.106
Morgan County	55,920	0.103	0.102	0.107
Shelby County	40,307	—	—	—
All of Indiana	5,544,160	0.127	0.140	0.120
All of Illinois	11,430,603	0.120	0.122	0.128
All of Kentucky	3,685,297	0.126	0.133	0.124
All of Michigan	9,295,298	0.123	0.136	0.121
All of Ohio	10,847,116	0.124	0.136	0.144
All of United States		0.105	0.110	0.107

[1] Population based on 1990 census.
[2] — , no data reported.

SOURCE: U.S. EPA 2001f. "AIRData - Monitor Summary Report."
Available at: http://www.epa.gov/air/data.html.
Last updated 3/28/2000;
Retrieved 7/09/2000.

3.1.2 Nitrogen Dioxide

Nitrogen dioxide, which is one of seven nitrogen oxides that are present in the ambient air, is a highly reactive reddish-brown gas. In addition to participating in the reactions leading to the formation of ozone and smog, nitrogen dioxide readily reacts with water vapor in the atmosphere to produce nitric acid. Nitrogen dioxide also absorbs visible light and contributes to decreases in visibility. Nitrogen dioxide is produced by the incomplete combustion of fossil fuels.

One nitrogen dioxide monitoring site met the study criteria for completeness. This monitor, which is located in Indianapolis (Marion County), represents residential land use in an urban/center city location. It generates instantaneous nitrogen dioxide measurements that are reported as hourly averages and as 24-hour mean observations. During the period of study, the percent of missing data was 0.9 percent at this site. Three additional monitoring sites, located in Hendricks County and having only one year of measurements, were excluded from the study because they did not meet the study criteria.

The daily mean and daily 1-hour maximum nitrogen dioxide levels for Indianapolis averaged over the study period were 0.016 ppm and 0.007 ppm, respectively (Table 3-2). The historical record of compliance shows that Indianapolis has been in compliance with the primary NAAQS for nitrogen dioxide, which is 0.053 ppm expressed as an annual arithmetic average not to be exceeded (U.S. EPA 2001a). The average annual nitrogen dioxide concentrations measured during the study period (Table 3-4), which are about three times lower than the NAAQS, are indicative of good air quality. The annual nitrogen dioxide levels are comparable to average levels reported for the United States, and somewhat lower than levels reported for Indiana and other states in the region.

Table 3-4: Summary of Annual Nitrogen Dioxide Levels in Marion County, Adjacent States, and the United States

Area	Population[1]	Annual Average Nitrogen Dioxide Concentration (ppm)		
		1997	1998	1999
Marion County	797,159	0.015	0.019	0.018
All of Indiana	5,544,160	0.020	0.029	0.033
All of Illinois	11,430,603	0.034	0.032	0.032
All of Kentucky	3,685,297	0.020	0.023	0.022
All of Michigan	9,295,298	0.026	0.023	0.024
All of Ohio	10,847,116	0.028	0.029	0.029
All of United States		0.018	0.018	0.018

SOURCE: U.S. EPA 2001f. "AIRData - Monitor Summary Report." Available at: http://www.epa.gov/air/data.html. Last updated 3/28/2001;
Retrieved 7/09/2001.
[1] Population based on 1990 census.

3.1.3 Sulfur Dioxide

Sulfur dioxide is a highly reactive, colorless gas with a pungent, irritating odor that is produced primarily by the combustion of coal and oil. The primary indoor sources include combustion sources that burn sulfur-containing fuels (such as kerosene heaters and leaks from damaged or improperly maintained combustion furnaces).

All four of the sulfur dioxide monitoring sites that meet the study criteria for completeness are located in Marion County. The monitoring sites represent agricultural, residential, commercial land use in rural and urban/center city locations. These monitors generate instantaneous sulfur dioxide measurements that are reported as hourly averages and as 24-hour mean observations. The percent of missing data was less than 1 percent at each of the sites. Additional monitors were located in Morgan (data for 1997) and Hendricks counties (data for 1998 and 1999), but these sites were excluded from the study because each had high percentages of missing data.

During the study period, the 24-hour mean and daily 1-hour maximum sulfur dioxide levels for Marion County were 0.005 ppm and 0.033 ppm, respectively (Table 3-1). The measured average 24-hour concentrations and annual concentrations were about five times below the corresponding NAAQS standards of 0.14 ppm and 0.03 ppm, respectively (U.S. EPA 2001a) (Table 3-5), and these levels are indicative of good air quality as measured by the 24-hour sulfur dioxide AQI levels (0.0 ppm – 0.03 ppm) (U.S. EPA 2001c). Sulfur dioxide levels in the study region are comparable to those reported for the United States as a whole, but generally lower than those reported for Indiana and other states in the region.

3.1.4 Particulate Matter, Lead, and Carbon Monoxide

Particulate matter, which includes organic compounds and inorganic compounds such as lead and sulfate aerosols, is produced by a variety of processes including combustion processes, industrial emissions, and chemical reactions in the atmosphere. Particles less than 10 microns in size are of greatest concern because these particles can be inhaled deep into the respiratory tract. Carbon monoxide is a colorless, odorless, and nonreactive gas that is produced by the incomplete combustion of fossil fuels, primarily from transportation sources.

Particulate matter PM10 (aerodynamic diameter less than 10 microns), lead, and carbon monoxide were excluded from the study, primarily because of deficiencies in the air monitoring database.

Table 3-5: Summary of Annual Mean and 2nd Highest 24-Hour Sulfur Dioxide Levels in Marion County, Adjacent States, and the United States

Area	Population[1]	Sulfur Dioxide Concentration (ppm)					
		2nd Maximum 24-hr			Annual Mean		
		1997	1998	1999	1997	1998	1999
Marion County	797,159	0.030	0.024	0.024	0.006	0.005	0.007
All of Indiana	5,544,160	0.083	0.071	0.110	0.017	0.015	0.015
All of Illinois	11,430,603	0.063	0.087	0.065	0.010	0.012	0.009
All of Kentucky	3,685,297	0.037	0.045	0.056	0.009	0.009	0.008
All of Michigan	9,295,298	0.044	0.073	0.053	0.008	0.012	0.009
All of Ohio	10,847,116	0.072	0.070	0.065	0.012	0.011	0.011
All of United States		0.025	0.024	0.023	0.005	0.005	0.005

[1] Population based on 1990 census.
SOURCE: U.S. EPA 2001f. "AIRData - Monitor Summary Report."
Available at: http://www.epa.gov/air/data.html. Last updated 3/28/2001;
Retrieved 7/09/2001.

Particulate matter, which is collected every sixth day, has been identified as a potentially important variable in the literature review, and it should be considered for inclusion in future studies. Because the particulate data are collected every sixth day, the data will require further handling to adjust for missing data in order to include it in future studies. There are seven sites (one in Anderson and six in Indianapolis) that meet the study criteria for three years of data. These sites include three industrial sites, two commercial sites, one residential site, and one agricultural site in rural, suburban, and urban/center city locations.

Lead has not been identified as an important variable in the literature review, and therefore, it was excluded from the analysis. There are four sites that monitor for lead and meet the study criteria for three years of data. Three of the sites are industrial in rural locations and the fourth is a residential site in a rural location.

Carbon monoxide data were not included in the study because concentrations are low and relatively homogeneous in the study area and because it has not been found to be important in the literature. There were two carbon monoxide locations, both located in Indianapolis, which had three years of data. One of these locations was a commercial urban/center city site and the other was a residential urban/center city site.

3.2 Meteorological Measurements

The meteorological measurements included in the study (temperature, relative humidity, and dew point) were obtained from the National Weather Service Indianapolis International Airport weather station. Table 3-6 provides a comparison between average monthly temperatures and total monthly precipitation during the study period to long-term monthly data. A summary of the meteorological data for the period of study is shown in Table 3-7. The daily mean meteorological parameters had 16.7 percent missing data, and this percentage increased to 26.6 percent and 35.2 percent for the 2-day and 3-day mean. Methodologies to reduce these data gaps should be explored in future studies. The mean of the monthly temperatures during the study period were lower in 1997 (68 ^{o}F) than in 1998 (72 ^{o}F) and 1999 (72 ^{o}F). Additional monitoring stations were available for the meteorological variables; however, they were excluded from the study because of the high percentage of missing data.

Table 3-6: Comparison of Average Monthly Temperatures and Precipitation during the Study Period to Long-term Trends at the Indianapolis International Airport Weather Station[1]

Month	Average Temperature (°F)				Monthly Precipitation (in.)			
	Study Area			Long-term Average[2,3]	Study Area			Long-term Average[2,3]
	1997	1998	1999		1997	1998	1999	
May	56.7	67.0	64.3	61.1 – 64.1	4.9	6.1	3.8	2.7 – 4.6
June	69.6	71.5	73.7	72.8 – 70.8	3.2	10.3	2.6	2.7 – 3.9
July	75.3	74.8	79.2	74.4 – 76.2	0.6	4.0	3.0	3.3 – 5.1
August	71.6	75.3	72.4	72.2 – 74.0	3.0	3.7	1.5	2.4 – 4.2
September	66.0	71.4	67.0	65.5 – 67.7	1.5	0.5	0.8	1.8 – 3.3

[1] Operated by the National Weather Service; for the period May 1 - September 30.
[2] Long-term averages taken from "NWS Climate Table." (National Weather Service 2001) Available at: http://www.nws.noaa.gov/climatex.html. Authored by Jim Fexix. Last modified 8/13/1998; Retrieved 10/27/2001.
[3] Values from the study area that are within the long-term average are considered to be within the normal variation.

Table 3-7: Summary of Meteorological Variables at the Indianapolis International Airport Weather Station, 1997-1999[1]

Variable	No. Obs.	Percent Missing Data	Mean	SD	Percentile								
					Min	5th	10th	25th	50th	75th	90th	95th	Max
Temperature (°F)													
daily max	455	0	79.4	8.6	55	63	66	74	81	86	89	91	99
daily min	455	0	61.2	8.3	33	45	49	56	62	67	71	73	78
daily mean	379	16.7	70.8	7.7	48	56	59	66	73	76	79	81	87
2-day moving ave	334	26.6	70.8	7.4	49	57	60	66	72	76	79	81	85
3-day moving ave	295	35.2	70.7	7.2	52	57	61	66	72	76	78	81	84
Relative Humidity (%)													
daily max	455	0	91.6	8.7	58	73	80	88	93	100	100	100	100
daily min	455	0	51.5	14.5	22	29	32	41	52	61	71	78	90
daily mean	379	16.7	71.1	11.7	39	51	54	62	72	79	85	90	96
2-day moving ave	334	26.6	71.0	10.4	41	53	56	64	72	78	84	87	92
3-day moving ave	295	35.2	70.9	9.5	43	53	57	64	72	78	82	86	89
Dew Point (°F)													
daily max	455	0	63.8	9.3	35	46	51	57	65	71	75	76	82
daily min	455	0	55.3	10.2	18	37	41	49	56	63	68	70	75
daily mean	379	16.7	59.8	9.8	29	42	46	54	61	68	72	73	76
2-day moving ave	334	26.6	59.8	9.3	30	43	47	54	61	67	71	73	76
3-day moving ave	295	35.2	59.8	9.0	33	42	47	55	61	67	70	73	75

[1] Operated by the National Weather Service; for the period May 1 - September 30, 1997-1999.

4. DESCRIPTION OF THE STUDY

Section 4 describes the design for the epidemiologic study of hospital records of children in the central Indiana study area for the summers of 1997 through 1999. This section includes descriptions of the study area, study population, hospital admissions data, the dependent variable, the explanatory variables, and the statistical methodology. Appendix C, Indianapolis Asthma Study Codebook, contains information about the data set used in this study and reports on the classification and coding of each variable.

4.1 Study Area

The study area included the Indianapolis Metropolitan Statistical Area (MSA), which consists of nine counties in central Indiana—Boone, Hamilton, Hancock, Hendricks, Johnson, Madison, Marion, Morgan, and Shelby. Because the City of Indianapolis has county-wide government, "Indianapolis" has the same boundaries as Marion County (Figure 3-1).

4.2 Study Population

Epidemiologic studies generally make a distinction between the target population and the study population. The target population is the conceptual, or ideal, population that one wishes to study; the study population is the one actually used for the research project. In most epidemiologic studies, the target and study populations overlap, but are not identical.

The target population of all studies conducted for the Central Indiana Asthma Research Project, including the Indianapolis Asthma Study, is all children, ages 1 to 17 years, present in the study area during the summers of 1997 through 1999. Infants younger than one year of age are not included because of the difficulty of making an asthma diagnosis in this age group. The study population, the one actually studied for the Indianapolis Asthma Study, is a subset of the target population, because it includes only those children meeting the above criteria and who were admitted to one of the 20 area hospitals included in this study.

The study population excludes children who experienced asthma or other respiratory symptoms but were not admitted to a metropolitan area hospital. This group includes children who did not receive treatment or had self-treatment and those who were treated elsewhere, including as an outpatient, at a hospital emergency room, or at some other place (physician's office, at home, outside of the Indianapolis area, and so forth). Although the Indianapolis Asthma Study sought to include outpatient data—including visits to the emergency room—practical limitations on the availability of or access to these data, study resources, and time constraints only allowed for the analysis of data from this more restricted study population. Additional comments about the study population are found in Section 5 STRENGTHS AND LIMITATIONS OF THE STUDY and Section 7 CONCLUSION.

4.2.1 Hospital Admissions Data

The Indiana Hospital and Health Association (IHHA) provided the hospital admissions data used in this study. These data were provided to IHHA by twenty member hospitals in the nine-county Indianapolis metropolitan area. The hospitals participating in the study are as follows: Community North, Indianapolis; Community South, Indianapolis; Community East, Indianapolis; Community-Anderson, Anderson; Hancock Memorial, Greenfield; Hendricks Community, Danville; Johnson Memorial, Franklin; Major, Shelbyville; Methodist, Indianapolis; Morgan County Memorial, Martinsville; Riley Children's, Indianapolis; Riverview, Noblesville; St. Vincent Mercy, Elwood; St. John's, Anderson; St. Vincent's, Indianapolis; St. Vincent's-Carmel, Carmel; St. Francis, Mooresville; St. Francis, Indianapolis; Wishard, Indianapolis; and Witham Memorial, Lebanon.

The data set contains a record for each child admitted to an Indianapolis area hospital from May 1 through September 30 (referred to throughout this study as "summer") for calendar years 1997 through 1999. Children with home address ZIP codes outside of the metropolitan area or who were not admitted between May 1 and September 30 of the study years are excluded from the data set.

4.3 Dependent Variable

The dependent variable DIAG3 (diagnosis) classifies the diagnosis of each child's hospital admission record into one of three categories—Asthma, Other Respiratory, and Other Diagnosis—based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) (2001) reported in each record.

Each patient record contained a primary diagnosis field (DIAG01) and 10 or more secondary diagnoses (DIAG02 through DIAGnn). For the purposes of this study, a patient was categorized as an asthma case if any one of the ICD-9 codes in the patient record were 493 (including any fourth and fifth digit extension). The remaining records in the database were then classified as Other Respiratory cases based on the occurrence of one or more ICD-9 codes for respiratory infections; conditions for the upper or middle respiratory tract, conditions of the lower respiratory tract, respiratory symptoms, and/or other respiratory classifications.[10] The remaining records, which contain all other diagnostic codes, comprise the Other Diagnosis category.

Table 4-1 summarizes the classification scheme for the diagnostic categories. Each record was classified into one of the classes using a hierarchical coding process based on the codes listed in Table 4-1. This means that asthma cases (code 10) were classified before the higher codes (20 through 88).

Table 4-1: Classification of Diagnostic Codes

DIAGCAT[1]	Description (DIAGCATC)
10	Asthma
20	Possibly Asthma
30	Respiratory Infections, Upper Tract
40	Respiratory Infections, Middle and Lower Tract
50	Noninfectious Respiratory Conditions, Upper Tract
60	Noninfectious Respiratory Conditions, Middle and
70	Other Diseases of the Lung
80	Respiratory Symptoms
88	Other Diagnoses

[1]Category 20 Possibly Asthma is not used in this study. Categories 30 through 80 are combined into the Other Respiratory Diseases category. The analysis variable used in the study is DIAG3.

[10] The ICD-9-CM codes in these categories included selected codes from 460-466, 470-478, 480-487, 490-496, 510-519, 748, 786, 011-012, 079, 277. Further documentation for the coding hierarchy is contained in a project documentation codebook, "Methodology for Coding Asthma and other Respiratory Disease States." July 2001.

The coding methodology was applied as follows: Each case was first set to a value of "88," the Other Diagnosis category. The Asthma cases were then removed first, recoding them to "10." Next, the remaining records were then classified into the Other Respiratory category (codes 30, 40, 50, 60, 70, and 80). The Other Diagnosis category (code 88) consists of all other diagnostic codes other than those classified into the Asthma and Other Respiratory categories, as well as missing data and invalid codes.

The Possible Asthma category referred to in Table 4-1 is a diagnostic category reserved for future studies. Anecdotal evidence suggests that some physicians may misclassify asthma cases as "bronchitis" or other respiratory conditions, even though their prescribed treatment (bronchodilators and anti-inflammatory medications) is consistent with a diagnosis of asthma. The possible reasons for this misclassification of asthma cases appear to be complex. Some possible explanations are that physicians may avoid the use of the asthma ICD codes because of concerns about a patient not receiving insurance coverage for asthma, and because some non-specialists may lack sufficient knowledge about the symptoms distinguishing asthma from bronchitis and other respiratory diseases to classify the disease properly.

Since the IHHA database does not include medications prescribed by the attending physician, the Possibly Asthma category could not be included in the Indianapolis Asthma Study. Other studies done under the umbrella of the Central Indiana Asthma Research Project may use this category to study the under-reporting or misreporting of asthma.

4.4 Explanatory Variables

The explanatory variables, grouped into three classes, are used to "explain" the diagnosis. The three classes of explanatory variables are environmental measures (air quality and meteorological variables), social effects measures, and confounding measures.

4.4.1 Environmental Conditions Variables

The environmental conditions measures include the air quality and meteorological variables that are described and summarized in Section 3. The air quality measures analyzed in Section 6 are ozone, nitrogen dioxide, and sulfur dioxide. The air quality data, which were provided by IDEM, included nine ozone sites, one nitrogen dioxide site, and four sulfur dioxide sites.

The analysis strategy included four measures of ozone, nitrogen dioxide, and sulfur dioxide:

- daily maximum value (highest one-hour average for each day at each site),
- daily mean (24-hour average of the individual one-hour averages for each day at each site)
- 2-day mean (a moving average of the mean daily ozone concentrations for the 48 hours prior to the hospital visit)
- 3-day mean (a moving average of the mean daily ozone concentrations for the 72 hours prior to the hospital visit)

A daily mean was considered to be missing for the environmental measures if the number of valid hourly observations was less than 20.

An important methodological issue for this study is correctly representing the exposure to the air quality variables that each subject in the study area received. This issue is complicated by the lack of knowledge about the exposure time of each child, the child's activity level, and whether the child traveled from place to place during the time preceding the visit to the hospital. A major assumption in this study is that each child's primary exposure location is the home address (ZIP code area) given at the time of the hospital visit.

For ozone, it is assumed that the concentration that is most representative of the child's exposure is the ozone monitoring location that is nearest to the child's home address, calculated as the centroid of the ZIP code coordinates using Geographical Information System (GIS) technology. It is recognized that this assumption provides only an approximation to the true exposure. Subsequent work will refine this portion of the overall methodology.

Nitrogen dioxide exposures were determined by matching each patient's date of admission to measurements from a single monitoring site located in Indianapolis. An important methodological issue is the adequacy of using a single site to represent the nine-county metropolitan area's nitrogen dioxide levels. Nitrogen dioxide, along with hydrocarbon emissions, plays a key role in the formation of ozone and other constituents in smog. The primary sources of nitrogen dioxide are high temperature combustion sources, such as automobiles and power plants, which release nitric oxide that is readily converted to nitrogen dioxide in the atmosphere. Because of the differences in sources between ozone and nitrogen dioxide, it is likely that nitrogen dioxide levels may vary more spatially, and a single monitor may not capture this variability.

Sulfur dioxide exposures were determined by matching each patient's date of admission to the average sulfur dioxide level calculated among the four monitoring locations used in the study. An important methodological issue for sulfur dioxide is the adequacy of using the average of four monitors in one county to represent a nine-county geographical area with a diverse mix of properties and emissions points. Sulfur dioxide is a localized pollutant that is emitted from combustion sources, such as power plants and metallurgical process, which utilize sulfur-containing fuels. Greater geographical coverage would provide a better estimation of individual exposure levels.

Meteorological data from the National Weather Service's station at the Indianapolis International Airport were used for the analysis. The analysis strategy for meteorological data included five measures of temperature, relative humidity, and dew point:

- daily maximum (highest one-hour observation for each day)
- daily minimum (lowest one-hour observation for each day)
- daily mean (24-hour average of the individual one-hour observations for each day)
- 2-day mean (a moving average of the daily mean for the 48 hours prior to the hospital visit)
- 3-day mean (a moving average of the daily mean for the 72 hours prior to the hospital visit)

A daily mean was considered to be missing if the number of hourly observations was less than twenty. Each patient's day of admission was matched to the daily readings. An important methodological issue for the meteorological variables is the adequacy of using a single monitor to represent meteorological conditions throughout the nine-county area.

4.4.2 Social Effects Variables

The social effects variables are Age, Race/ethnicity, Sex, and Income. Each has been identified in the literature as associated with asthma. Information for each of the social effects variables was contained in the IHHA hospital records database. Race/ethnicity is classified as white and nonwhite in this study. Variations in the coding of race and/or ethnicity among the twenty hospitals allowed for this level of detail only. Income is measured by the estimated Median Household Income in 1999 that was associated with the patient's ZIP code.

4.4.3 Confounding Variables

Confounding variables were introduced in this analysis to adjust for the self-selection effects inherent in this type of study design. Confounding variables represent "extraneous" conditions that may affect the relationship of diagnosis to the other explanatory variables of interest—namely, environmental measures and social measures. Confounding effects arise in epidemiologic studies of this type because of the non-experimental nature of the study design, in which the researchers are unable to control the characteristics of the subjects and other factors by randomly assigning subjects to study groups. Rather, researchers must examine data that are the result of "history" and other circumstances beyond their control. Including confounding variables in the analysis strengthens the findings based on the other variables of interest. For additional information on the use of confounding variables in epidemiologic studies, see Kleinbaum and others (1982, 242-265). The effects of each explanatory variable are examined below with simple models.

The confounding variables examined are the weekday when admitted and emergency room use. The emergency room effect is a dichotomous variable indicating whether patients were admitted after first using the emergency room or visiting the hospital as an outpatient. Routine admissions and transfers are grouped into a category, other. This variable does not contain information on children who used the emergency room or were outpatients, but were not admitted to the hospital.

4.5 Statistical Methodology

The analysis used to explain the diagnosis (DIAG3) is a Multinomial Logit Model, as described by Agresti (1990, pp. 306-346). Each model contains two logit functions on the left side of the equation representing the logit of the Asthma versus the Other Diagnosis categories and the logit of the Other Respiratory Disease versus the Other Diagnosis. The third category of the variable DIAG3, Other Diagnosis, is used throughout the analysis as the base category.

The two logit functions estimated in the analyses and reported below (Section 6) are as follows:

(1) Logit(Asthma/Other Diagnosis) = log(∏(Asthma)/ ∏(Other Diagnosis))

(2) Logit(Other Respiratory Disease/Other Diagnosis) =
log(∏(Other Respiratory Disease)/ ∏(Other Diagnosis))

The right side of the equation includes estimated effects of the explanatory variables—namely, environmental, social, and/or confounding. The levels of the explanatory variables define subpopulations, within which the logit functions are estimated from the data. The data are arrayed as an r x c contingency table, where r is the number of subpopulations formed by the levels of the explanatory variables, and c equals 3, the number of categories in the dependent variable DIAG3. The entries in the contingency table are frequencies (counts) from which the estimated probabilities prc are calculated. In sum, each analysis involves estimating two logit functions for two or more subpopulations.

An example of a multinomial logit analysis is the one determining the effects of sex (male, female) on the diagnosis. This analysis is based on a 2 x 3 contingency table, which produces 4 estimated parameter values:

(1) The mean effect for logit (1)

(2) The sex effect given logit (1)

(3) The mean effect for logit (2)

(4) The sex effect given logit (2)

For this example, the results presented in this report are the estimated probabilities of asthma or other respiratory disease diagnoses for each sex. These estimated probabilities are calculated by the statistical software from the final model. For saturated models, the estimated and observed probabilities are identical -- that is, all degrees of freedom are used to estimate the effects. The statistical analyses were done using the CATMOD procedure in the SAS software (Stokes and others 2000).

5. STRENGTHS AND LIMITATIONS OF THE STUDY

5.1 Strengths

The Indianapolis Asthma Study is unique in that it includes the population of records for all hospital admissions in the Indianapolis area. All of the research studies summarized in Appendix A are limited to frequencies (counts) of asthma diagnosis, and they include only aggregated counts of asthma, which are then analyzed by comparing them to averages of area pollutants. The advantage of the study design used here is the study's ability to estimate the magnitude of asthma relative to other respiratory diseases and other hospital admissions.

The study's strengths also include a large number of hospitals, multiple years of data (three years), multiple pollutants (ozone, sulfur dioxide, and nitrogen dioxide), meteorological parameters (temperature, relative humidity, and dew point), and social characteristics (age, race/ethnicity, income, and sex).

Another of the study's strengths is that multiple ozone monitoring locations are available, permitting a closer estimation of individual exposures. Subject exposure levels are estimated by using the monitor reading closest to the patient's home address ZIP code, rather than to an average of ozone concentration. The Indianapolis Asthma Study also considers several types of measures and averaging times. The air pollution measures are determined using state of the art equipment, and these data have been quality assured by IDEM.

5.2 Limitations

The study's limitations are primarily related to the patient and environmental databases. The IHAA hospital database contains limited information on hospital admissions only. Because the data set is limited to hospital admissions (inpatient records), all other visits for medical treatment (outpatient visits) are not included. The self-selection biases of limiting the study to children who are admitted to hospitals are unknown, but this study is likely to over-represent those with more severe illnesses requiring treatment that involves a hospital stay. Conversely, children who visited private physicians or emergency centers, which are widely located in the Indianapolis area, are not represented in the study.

The diagnosis and counts of the diagnosis also present limitations in this study. The study did not attempt to remove children with repeat admissions for the same asthmatic episode, and it is not know to what degree these repeat admissions may have resulted in over-counting. The study did consider a case to be asthma if one of the diagnostic codes was asthma, and it is possible that this resulted in over-counting. Another limitation of the hospital admissions database is that it does not include information about medications related to the treatment of asthma. This omission may underestimate the total asthma cases. Based on a study of one Indianapolis area hospital's medication records and anecdotal information provided by area physicians, the researchers believe that asthma is often misdiagnosed as bronchitis or another respiratory illness, but treated with medications commonly used for asthma patients. It is not known if misdiagnosis occurs more frequently in the outpatient setting where a lesser diagnosis justifies the office or in the hospital where a more substantive diagnosis justifies the admission. The authors believe the lack of medication data to be the most likely cause of erroneous counts of asthma cases and, as a consequence, asthma cases are probably underestimated in this study.

The environmental database also has some weaknesses. There is only one nitrogen dioxide monitor and four sulfur dioxide monitors to represent concentrations in the nine-county area. Particulate matter and pollen data were available, but could not be used because of missing data and other measurement issues.

6. FINDINGS

The findings reported in this section are derived from a process using both theoretical and statistical criteria. Because the primary focus of this study is on determining the importance of environmental conditions on children's health, environmental variables are analyzed first. After evaluating the importance of these environmental conditions on hospital admissions, the secondary explanatory variables measuring social effects are evaluated. Finally, the confounding variables arising from the lack of experimental controls are evaluated. The combination of these two criteria, theoretical relevance and statistical significance, are applied to the primary questions in this study to determine whether variables are included or excluded from the analysis.

The statistical criteria used to include or eliminate variables, referred to as effects on diagnosis, are statistical tests of significance and the explanatory power of the model. A Goodness of Fit (GOF) test is used first to determine whether the model explains the variation in admissions of children to hospitals in the study area. A GOF test that is statistically significant means that the model does not adequately explain the data. Therefore, statistical tests of the individual variable effects are unreliable and cannot explain admissions. Conversely, a non-significant GOF test ($\alpha = 0.05$) means that the model adequately explains the data and the individual variable effects may be estimated and used to explain admissions.

If the GOF test is not significant, the analysis then moves to another set of statistical tests to determine whether the individual effects -- for example, the Ozone Daily Mean -- explain a statistically significant percentage of variation in hospital admissions. For these individual effects tests, a less strict p-value is used ($\alpha = 0.10$). If the test of the effect is statistically significant, the analysis proceeds to test the effect within each logit model. In this analytical framework, three tests are potentially done. The ultimate goal is to produce a statistical model that includes theoretically important variables and has a non-significant GOF test. Additionally, the model should ideally include explanatory effects that meet the p-value $\alpha = 0.10$ criterion. One does not always find a theoretically relevant model that meets these strict statistical criteria.

Sections 6.1, 6.2, and 6.3 evaluate the explanatory power of environmental, social, and confounding effects, respectively for childhood asthma and respiratory illness. In these sections, the reader should note that all increases and decreases in probabilities are relative to the base case, Other Diagnosis.

6.1 The Effects of Environmental Conditions on Children

The following sections examine the separate effects of ozone, nitrogen dioxide, sulfur dioxide, dew point, temperature, and relative humidity on diagnosis. In each section, the separate measures of the environmental variables are examined, and two forms of the model are evaluated. The first form of the model is one where each explanatory variable is assumed to have ordered, linear categories (ordered model), and the second form is one where each variable is assumed to be categorical with no particular order (unordered) model. There is no GOF test in the unordered models for the environmental variables because these models are saturated.

6.1.1 Ozone Effects

Table 6-1 summarizes the eight simple models examined for each of the four ozone measures -- the Ozone Daily Mean, the Ozone Daily Maximum, the Ozone 2-day Mean, and the Ozone 3-day Mean, and two model structures. Among the four models with the ordered categories assumption, the Ozone Daily Mean is the best measure of the effect of ozone on children. The remaining three ordered models fail the GOF test and are thus eliminated from further consideration. The models without the ordered categories assumption show a statistically significant effect ($p < .05$) for each of the four measures -- the Ozone Daily Mean, Ozone Daily Maximum, Ozone 2-day Mean, and Ozone 3-day Mean.

The Ozone Daily Mean with the ordered categories (linear) assumption is the best of the five acceptable models. It explains a statistically significant amount of variation associated with asthma alone, but the negative association is contrary to the hypothesis derived from the research literature. In others words, as ozone concentrations increase, the probability of hospital admissions for asthma relative to the reference category (Other Diagnosis) decreases (Figure 6.1). There is no statistically significant effect of ozone on other respiratory diseases. The final model estimates that as ozone concentrations increase from about 0.015 ppm to 0.065 ppm, the estimated probability of an asthma admission declines from about 0.22 (22 percent) to 0.13 (13 percent).

The ozone concentrations in the Indianapolis study, which are good to moderate with some elevated days, were numerically higher for the categories of comparison than other studies that found a statistically significant negative association between ozone and asthma and higher than all but three of the studies that reported a statistically significant positive association between ozone and asthma.

Table 6-1: Summary of Statistical Tests for Four Ozone Measures and Two Model Structures[1]

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Ordered Categories										
Ozone Daily Mean	19.79	16	NS3	381.42	2	yes	32.18	2	0.0001	8.4%
Ozone Daily Maximum	25.50	16	NS	419.44	2	yes	13.98	2	LOF[4]	3.3%
Ozone 2-day Mean	29.63	16	0.0200	301.78	2	yes	36.91	2	LOF	—
Ozone 3-day Mean	30.90	16	0.0138	225.08	2	yes	58.04	2	LOF	—
Unordered Categories										
Ozone Daily Mean	saturated			4578.31	2	yes	53.69	18	0.0001	1.2%
Ozone Daily Maximum	saturated			4699.42	2	yes	39.50	18	0.0024	0.8%
Ozone 2-day Mean	Saturated			4554.34	2	yes	68.89	18	0.0001	1.5%
Ozone 3-day Mean	Saturated			4398.03	2	yes	92.51	18	0.0001	2.1%

[1]GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2]The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
[4] LOF = lack of fit.

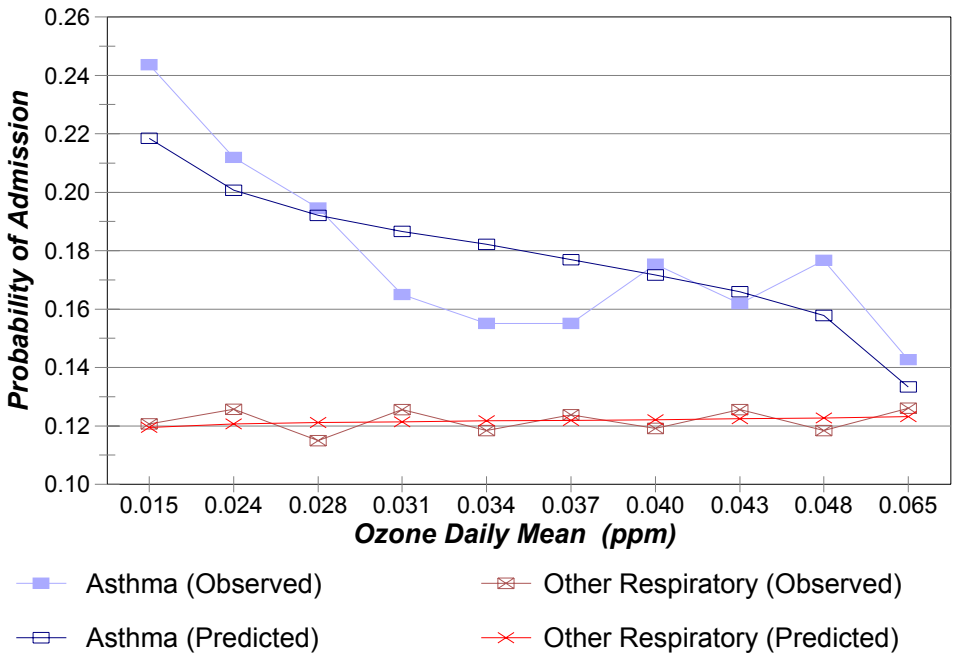

Figure 6-1: Ozone Daily Mean Effects on Admissions for Respiratory Illness

6.1.2 Nitrogen Dioxide Effects

The results reported in Table 6-2 suggest that nitrogen dioxide concentrations played an important role in children's hospital admissions. The pattern of statistical tests shows that the percent of diagnoses for asthma increases with elevated nitrogen dioxide concentrations. The nitrogen dioxide effect holds for asthma only, but not for other respiratory diseases (Figure 6-2). Thus, the data for nitrogen dioxide provide evidence in support of the findings in the literature that increased nitrogen dioxide is associated with increased admissions for asthma, but the data do not support the research hypotheses for the category of other respiratory illnesses.

The nitrogen dioxide concentrations in the Indianapolis study, which were uniformly low and indicative of good air quality, were lower than roughly 2/3 of the studies that reported data and a statistically significant positive association between asthma and the oxides of nitrogen.

Table 6-2: Summary of Statistical Tests for Four Nitrogen Dioxide Measures and Two Model Structures

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	**DF**	**p ≤ .05**	**Chi-square**	**DF**	**p ≤ .05**	**Chi-square**	**DF**	**p ≤ .10**	**% Explained[2]**
Ordered Categories										
Nitrogen Dioxide Daily Mean	27.23	16	0.0390	752.02	2	yes	0.77	2	LOF[4]	—
Nitrogen Dioxide Daily Maximum	13.50	16	NS[3]	683.26	2	yes	1.37	2	NS	—
Nitrogen Dioxide 2-day Mean	25.63	16	NS	613.56	2	yes	0.66	2	NS	—
Nitrogen Dioxide 3-day Mean	35.96	16	0.0029	548.54	2	yes	0.50	2	LOF	—
Unordered Categories										
Nitrogen Dioxide Daily Mean	saturated			4535.00	2	yes	27.80	18	0.0652	0.6%
Nitrogen Dioxide Daily Maximum	saturated			4708.31	2	yes	14.84	18	NS	—
Nitrogen Dioxide 2-day Mean	saturated			4332.16	2	yes	25.80	18	NS	—
Nitrogen Dioxide 3-day Mean	saturated			4278.98	2	yes	35.70	18	0.0077	0.8%

[1]GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
[4] LOF = lack of fit.

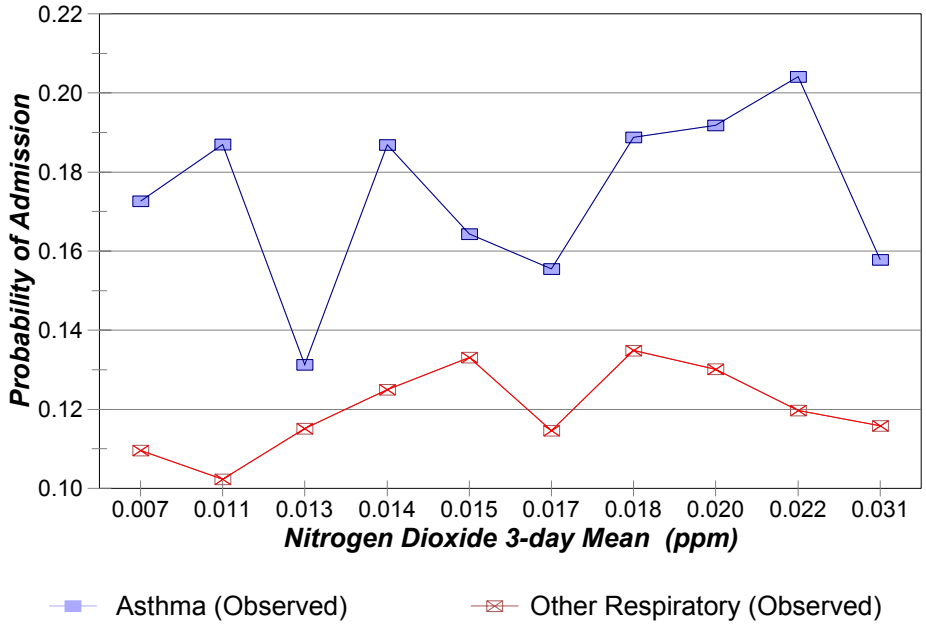

Figure 6-2: Nitrogen Dioxide 3-day Mean Effects on Admissions for Respiratory Illness

6.1.3 Sulfur Dioxide Effects

Sulfur dioxide does not appear to have a simple relationship to hospital admissions for asthma and other respiratory diseases. All of the ordered categories models fail the GOF test or do not explain a statistically significant amount of variation (Table 6-3). In the case of the unordered categories models, the statistical tests suggest that sulfur dioxide may play a role in hospital admissions. Three measures -- Sulfur Dioxide Daily Mean, Sulfur Dioxide 2-day Mean, and Sulfur Dioxide 3-day Mean -- explain a small, but statistically significant, amount of variation, and the Sulfur Dioxide 2-day Mean explains the most variation (3.7%).

Figure 6-3 shows that the Sulfur Dioxide 2-day Mean supports the research hypothesis that increased levels result in increased admissions for respiratory illness. This effect is statistically significant for asthma, but not for other respiratory illness.

The sulfur dioxide concentrations in the Indianapolis study, which were uniformly very low and indicative of good air quality, were lower than all but one of the studies that reported data and statistically significant positive associations between asthma and sulfur dioxide. The concentrations of roughly half of these studies, however, were only slightly higher than the concentrations in the Indianapolis study.

Table 6-3: Summary of Statistical Tests for Four Sulfur Dioxide Measures and Two Model Structures

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Ordered Categories										
Sulfur Dioxide Daily Mean	22.13	12	0.0361	1442.75	2	yes	5.76	2	LOF[4]	—
Sulfur Dioxide Daily Maximum	20.97	16	NS[3]	2045.11	2	yes	1.93	2	NS	—
Sulfur Dioxide 2-day Mean	28.94	12	0.0040	980.42	2	yes	17.33	2	LOF	—
Sulfur Dioxide 3-day Mean	13.80	8	NS	751.04	2	yes	12.83	2	0.0016	1.7%
Unordered Categories										
Sulfur Dioxide Daily Mean	saturated			3295.93	2	yes	27.78	14	0.0152	0.8%
Sulfur Dioxide Daily Maximum	saturated			4713.89	2	yes	22.64	18	NS	—
Sulfur Dioxide 2-day Mean	saturated			1285.81	2	yes	47.57	14	0.0001	3.7%
Sulfur Dioxide 3-day Mean	saturated			3945.53	2	yes	27.21	10	0.0024	0.6%

[1] GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
[4] LOF = lack of fit.

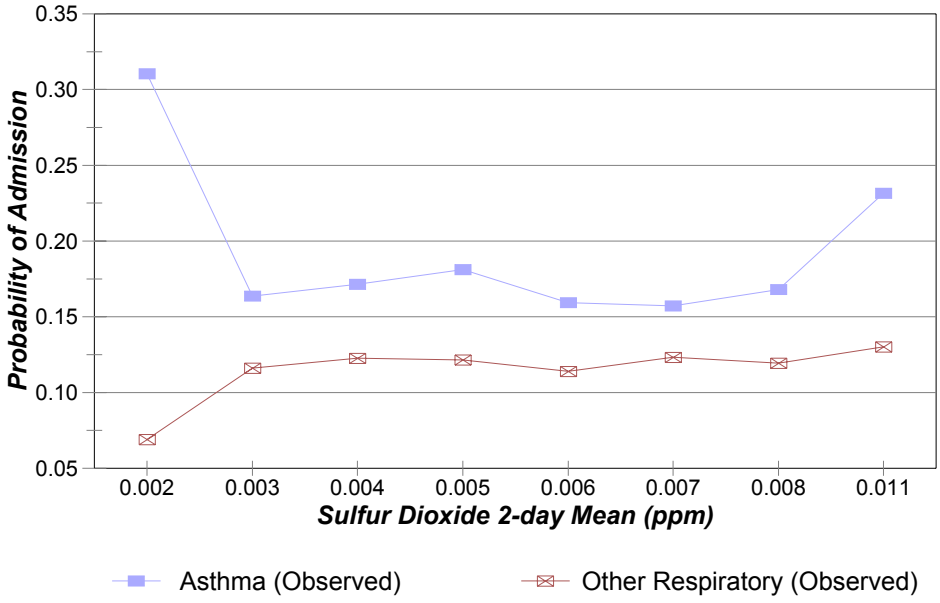

Figure 6-3: Sulfur Dioxide 2-day Mean Effects on Admissions for Respiratory Illness

6.1.4 Dew Point Effects

Table 6-4 shows that for the ordered categories models the Dew Point 2-day Mean meets the GOF test and explains the largest amount of variation (29.2%). The Dew Point Daily Maximum and the Dew Point Daily Minimum also meet the statistical criteria but explain a lesser amount of variation. For the unordered categories models each of the five Dew Point measures show some statistically significant, but small, association with diagnoses. Thus, the Dew Point 2-day Mean is the best explanatory measure for further analysis.

Figure 6-4 displays the effects of the Dew Point 2-day Mean measure on admissions to a hospital for either asthma or other respiratory illness. The figure demonstrates that as the Dew Point 2-day Mean increases, the probability of admission decreases for asthma. The effect of dew point on asthma admissions is statistically significant; the effect of the Dew Point 2-day Mean on other respiratory illness admissions is not statistically significant. In summary, there is a statistically significant negative (inverse) relationship for dew point on asthma.

Table 6-4: Summary of Statistical Tests for Five Dew Point Measures and Two Model Structures

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Ordered Categories										
Dew Point Daily Mean	26.73	16	0.0446	63.80	2	yes	17.79	2	LOF[4]	
Dew Point Daily Maximum	22.30	16	NS3	63.67	2	yes	11.69	2	0.0029	15.5%
Dew Point 2-day Mean	22.42	16	NS	50.20	2	yes	20.75	2	0.0001	29.2%
Dew Point 3-day Mean	25.76	16	NS	27.95	2	yes	28.23	2	0.0001	0.1%
Dew Point Daily Minimum	21.21	16	NS	132.14	2	yes	12.43	2	0.0020	8.6%
Unordered Categories										
Dew Point Daily Mean	saturated			3910.14	2	yes	44.70	18	0.0005	1.1%
Dew Point Daily Maximum	saturated			4618.83	2	yes	34.56	18	0.0107	0.7%
Dew Point 2-day Mean	saturated			3438.14	2	yes	42.72	18	0.0009	1.2%
Dew Point 3-day Mean	saturated			3042.88	2	yes	53.33	18	0.0001	1.7%
Dew Point Daily Minimum	saturated			4512.99	2	yes	34.06	18	0.0124	0.7%

[1] GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
[4] LOF = lack of fit.

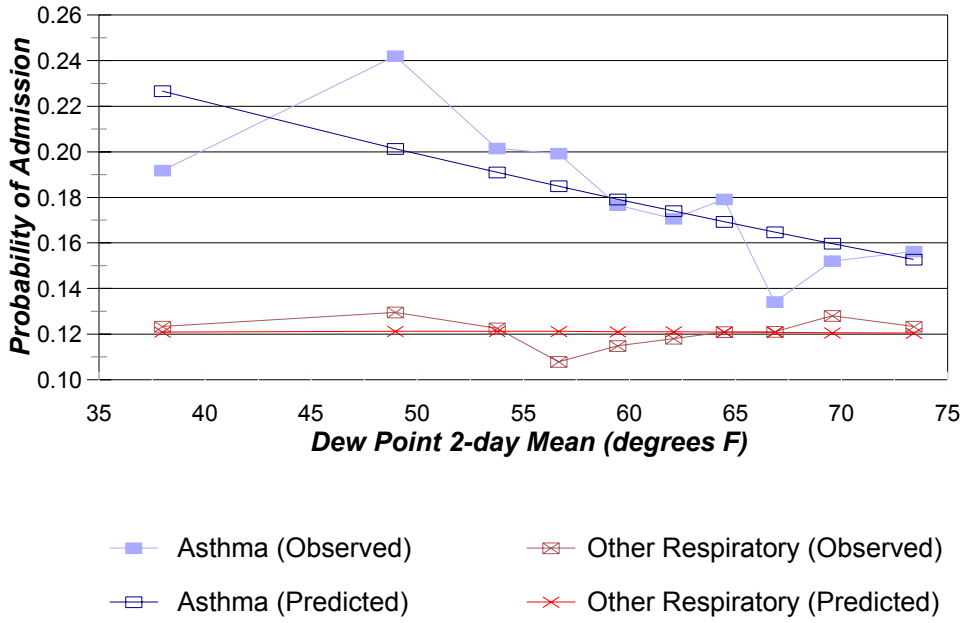

Figure 6-4: Dew Point 2-day Mean Effects on Admissions for Respiratory Illness

6.1.5 Temperature Effects

Because the dew point calculation uses both temperature and relative humidity, it is not an unexpected finding that temperature plays an important role in the diagnosis. Each of the five measures -- Daily mean, Daily Maximum, 2-day Mean, 3-day Mean, and the Minimum -- explain a statistically significant amount of variation for the unordered models (Table 6-5), and the Temperature Daily Minimum also has an ordered fit to the data and explains a large amount of variation (41.6 percent). Thus, temperature appears to play an important role in admissions for respiratory disease, and the Temperature Daily Minimum measure appears to be the best choice.

Figure 6-5 shows the effects of Temperature Daily Minimum on hospital admissions. The figure indicates that the probability of admission for asthma to an Indianapolis area hospital decreases as the daily minimum temperature increases. The analysis shows that admissions for asthma are more likely when the daily minimum is low and less likely when it is high (inverse relationship). This relationship is statistically significant. The model estimates that when the minimum daily temperature is about 40 ^{o}F, the admissions for asthma are about 23 percent. When the temperature is about 75 ^{o}F, the estimated admission rate for asthma is lower -- about 15 percent.

There is no statistically significant relationship between temperature and other respiratory admissions. As was found with the dew point measure, temperature plays a role in hospital admissions for asthma but not for other respiratory diseases.

Table 6-5: Summary of Statistical Tests for Five Temperature Measures and Two Model Structures

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Ordered Categories										
Temperature Daily Mean	33.97	16	0.0055	16.86	2	yes	21.40	2	LOF[4]	
Temperature Daily Maximum	27.60	16	0.0353	33.70	2	yes	6.71	2	LOF	
Temperature 2-day Mean	36.98	16	0.0021	16.96	2	yes	22.43	2	LOF	
Temperature 3-day Mean	30.97	16	0.0136	11.05	2	yes	24.41	2	LOF	
Temperature Daily Minimum	19.67	16	NS[3]	45.74	2	yes	32.53	2	0.0001	41.6%
Unordered Categories										
Temperature Daily Mean	saturated			3907.41	2	yes	55.08	18	0.0001	1.4%
Temperature Daily Maximum	saturated			3920.31	2	yes	34.57	18	0.0107	0.9%
Temperature 2-day Mean	saturated			3433.94	2	yes	57.74	18	0.0001	1.7%
Temperature 3-day Mean	saturated			3041.85	2	yes	53.06	18	0.0001	1.7%
Temperature Daily Minimum	saturated			4540.78	2	yes	51.13	18	0.0001	1.1%

[1] GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
[4] LOF = lack of fit.

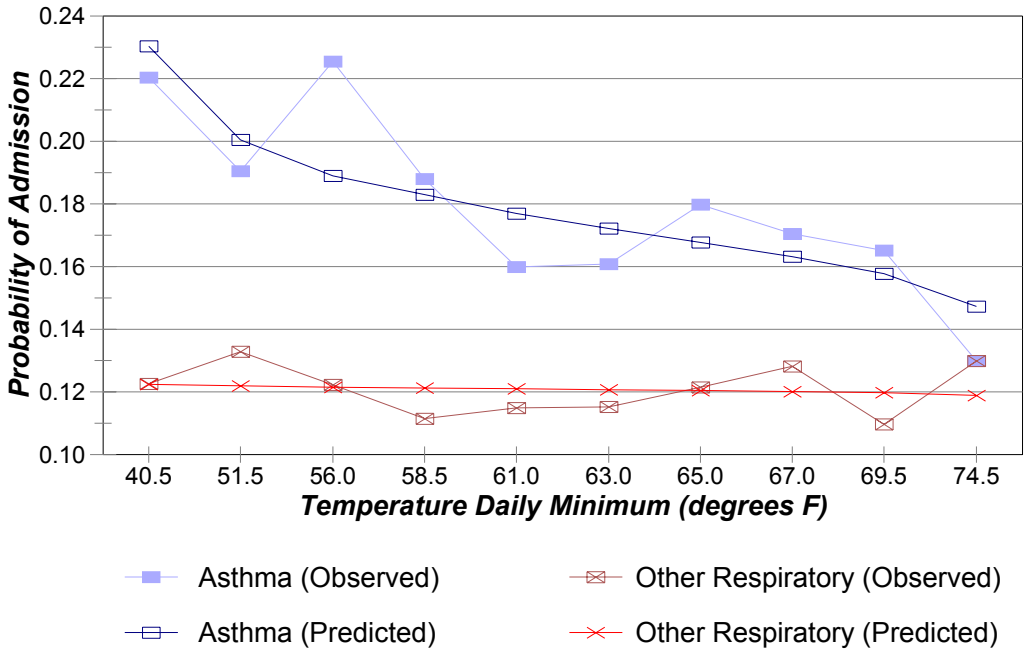

Figure 6-5: Temperature Daily Minimum Effects on Admissions for Respiratory Illness

6.1.6 Relative Humidity Effects

Table 6-6 shows that there is an association between relative humidity and diagnosis; the best measure is the Relative Humidity Daily Minimum. The Relative Humidity Daily Minimum variable using an ordered model fits the data and has a statistically significant amount of variation explained; however, the Daily Minimum measure is not significant for the unordered model. Three other measures -- Daily Maximum, 2-day Mean, and 3-day Mean -- also explain a significant, though small, amount of variation for unordered models. The Daily Minimum is the best indicator of relative humidity effects because the ordered model meets the GOF test criteria and also explains the most variation among the models.

Figure 6-6 shows a statistically significant negative (inverse) relationship between the Relative Humidity Daily Minimum and asthma admissions, but no statistically significant effect of relative humidity on admissions for other respiratory illness. The model estimates that when the relative humidity is about 27 percent, admissions for asthma are about 19 percent. When the relative humidity is about 80 percent, the estimated admission rate for asthma is lower -- about 16 percent.

Table 6-6: Summary of Statistical Tests for Five Relative Humidity Measures and Two Models

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Ordered Categories										
Relative Humidity Daily Mean	20.71	16	NS[3]	113.11	2	yes	1.47	2	NS	
Relative Humidity Daily Maximum	21.24	10	0.0195	57.83	2	yes	1.97	2	LOF[4]	
Relative Humidity 2-day Mean	41.26	16	0.0005	68.62	2	yes	4.35	2	LOF	
Relative Humidity 3-day Mean	33.02	16	0.0073	41.12	2	yes	6.72	2	LOF	
Relative Humidity Daily Minimum	14.94	16	NS	335.38	2	yes	5.48	2	0.0646	1.6%
Unordered Categories										
Relative Humidity Daily Mean	saturated			3907.68	2	yes	22.01	18	NS	
Relative Humidity Daily Maximum	saturated			4038.16	2	yes	22.62	12	0.0312	0.6%
Relative Humidity 2-day Mean	saturated			3433.32	2	yes	44.19	18	0.0005	1.3%
Relative Humidity 3-day Mean	saturated			3044.53	2	yes	40.12	18	0.0020	1.3%
Relative Humidity Daily Minimum	saturated			4537.35	2	yes	21.01	18	NS	

[1] GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] NS = not statistically significant
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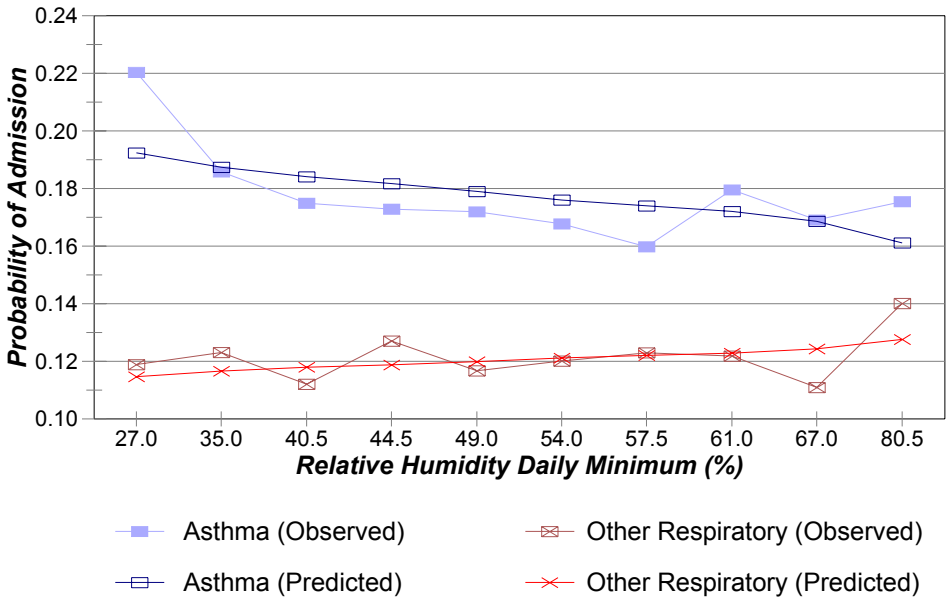

Figure 6-6: Relative Humidity Daily Minimum Effects on Admissions for Respiratory Illness.

6.1.7 Summary of Environmental Effects

The analyses reported in the previous sections provide information for setting priorities for including some variables and eliminating others from further analyses. Table 6-7 summarizes the findings for the six environmental measures. For ozone, the data support a finding that is contrary to the hypothesis -- namely, that hospital admissions for asthma decrease as ozone levels increase. There is no support from the Indianapolis data for the research hypothesis that increased ozone levels result in increased admissions for other forms of respiratory disease.

Table 6-7: Choice of Environmental Measures and Summary of Statistical Tests

Environmental Measure	Best Measure	Research Hypothesis	Research Hypothesis Supported?
Ozone	Daily Mean ordered categories	a positive relationship between ozone and asthma	a statistically significant negative association for asthma; no relationship for other respiratory diseases
Nitrogen Dioxide	3-day Mean unordered categories	a positive relationship between nitrogen dioxide and asthma	a statistically significant positive association for asthma; no relationship for other respiratory diseases
Sulfur Dioxide	2-day Mean unordered categories	a positive relationship between sulfur dioxide and asthma	a statistically significant positive association for asthma; no relationship for other respiratory diseases
Dew Point	2-day Mean ordered categories	insufficient research findings; no hypothesis	a statistically significant negative association for asthma; no relationship for other respiratory diseases
Temperature	Daily Minimum ordered categories	a positive relationship between temperature and asthma	a statistically significant negative association for asthma; no relationship for other respiratory diseases
Relative Humidity	Daily Minimum ordered categories	insufficient research findings; no hypothesis	a statistically significant negative association for asthma; no relationship for other respiratory diseases

For nitrogen dioxide the 3-day Mean measure using an unordered categories model suggests a positive association between nitrogen dioxide and asthma admissions, a finding consistent with the research hypothesis. The data, however, do not support the research hypothesis that increased nitrogen dioxide admissions result in increased admissions for other respiratory illnesses.

The findings for sulfur dioxide are similar to those reported for nitrogen dioxide. There is support for the research hypothesis of a positive association between sulfur dioxide levels and asthma admissions, but no support for admissions for other respiratory illnesses.

For dew point, temperature, and relative humidity the findings follow a consistent pattern for each measure. All three measures show a statistically significant, negative (inverse) relationship between the measure and asthma admissions. In other words, increased dew point levels, higher daily minimum temperatures, and greater daily minimum relative humidity are associated with lower levels of hospital admissions for asthma. The literature review indicated weak support for the effects of temperature on asthma, but there were insufficient numbers of studies on dew point and relative humidity to form research hypotheses. The data also provide no support for the research hypotheses that as dew point, temperature, or relative humidity rise, admissions for other respiratory illnesses also rise.

6.2 Social Effects

The effects of four social conditions -- Race/ethnicity, Sex, Age in years, and Income -- on diagnoses are discussed in this section. Each social effect is first examined in a simple, two variable model to determine whether admissions may be associated with it. Then, alternative models containing the best social variable predictors are combined into selected multivariate models.

6.2.1 Simple Social Effects Models

Table 6.8 summarizes six simple models of the effects of social effects on hospital diagnoses. A comparison of the explanatory effects of these models reveals that each has some explanatory value, but that the Age and Race/ethnicity variables have the greatest utility for further analysis. The table also reports on two additional ordered models for Age and Income. Both models did not meet the GOF criteria, and thus are eliminated from further analysis.

The relationship of age to admissions is shown in Figure 6.7. The data support the research hypothesis that as children age, the probability of admission to a hospital for asthma or other respiratory diseases declines. The data show that children ages 1 to 3 years are most at risk for being admitted for asthma, followed next by children in the 4 through 8 year group, children in the 9 to 14 years group, and lastly, the group 15 to 17 years. Thus, the relationship declines in a stepwise fashion and younger children are at greater risk than older children.

A similar pattern emerges for other respiratory admissions, but the age thresholds differ. For this type of disease, the relevant age groupings are 1 to 2 years, 3 to 10, 11 to 15, and 16 to 17 years. As with asthma the probability of admissions declines as children grow older.

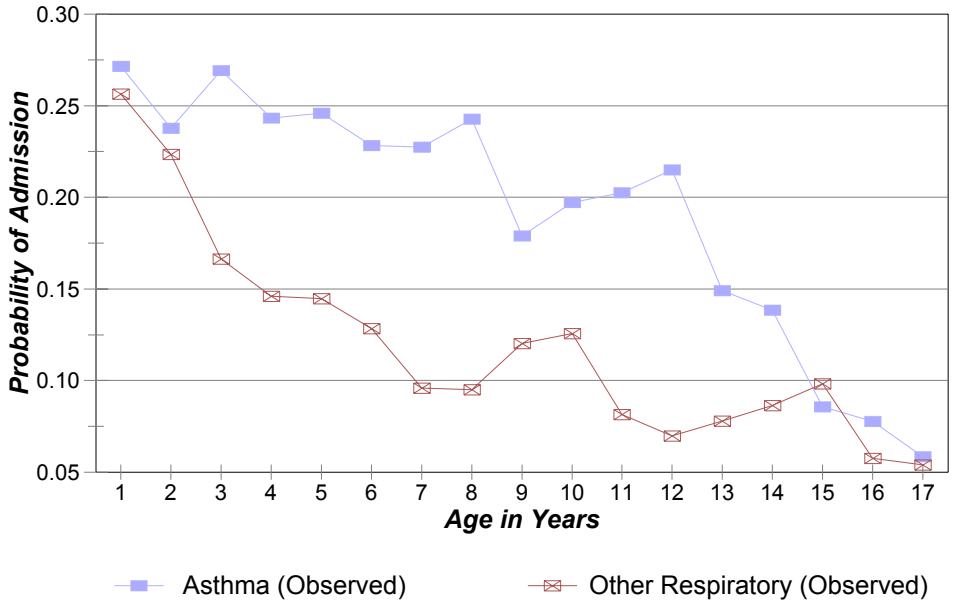

Figure 6-7: Age Effects on Admissions for Respiratory Illness

The data show a statistically significant difference for the effects of Race/ethnicity on admissions for any form of respiratory disease. Figure 6.8 shows that nonwhite children are more likely to be admitted for asthma than white children, a finding consistent with the research literature ($p = 0.0001$). However, white children are more likely to be admitted for other respiratory illnesses, though this relationship is marginally significant ($p = 0.0711$).

The relationship between Income and diagnoses is presented in Figure 6.9. The figure indicates that as people with household incomes in the fourth (upper) quartile of the United States are less likely to be admitted for asthma. This relationship is weak, explaining a small amount of variation in admissions. Furthermore, it appears that Race/ethnicity, a stronger measure, is confounded with Income, since nonwhites on average have lower median household incomes than whites. Thus, Race/ethnicity appears to be the better measure of this social effect.

Table 6-8: Summary of Statistical Tests for Six Simple Social Effects Models

Explanatory Variable	GOF Test[1]			Intercept			Predictor			
	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .05	Chi-square	DF	p ≤ .10	% Explained[2]
Race/ethnicity				3919.24	2	yes	265.90	2	0.0001	6.4%
Sex	saturated			4697.33	2	yes	149.76	2	0.0001	3.1%
Age	saturated			3939.56	2	yes	801.97	32	0.0000	16.9%
Income	saturated			3265.59	2	yes	161.21	6	0.0001	4.7%
Ordered Categories										
Age	107.81	30	0.0001	174.40	2	0.0001	740.07	2	LOF[3]	--
Income	18.55	4	0.0010	490.07	2	0.0001	143.29	2	LOF	--

[1] GOF = Goodness of Fit test. The GOF test is statistically significant (α = 0.05). There is no GOF test for a saturated model.
[2] The Percent Explained (% Explained) measure approximates the portion of total variation in the Chi-square statistic explained by the effect. It is computed by dividing effect Chi-square by the Total Chi-square. This statistic is descriptive and does not produce a statistically valid p-value.
[3] LOF = lack of fit.

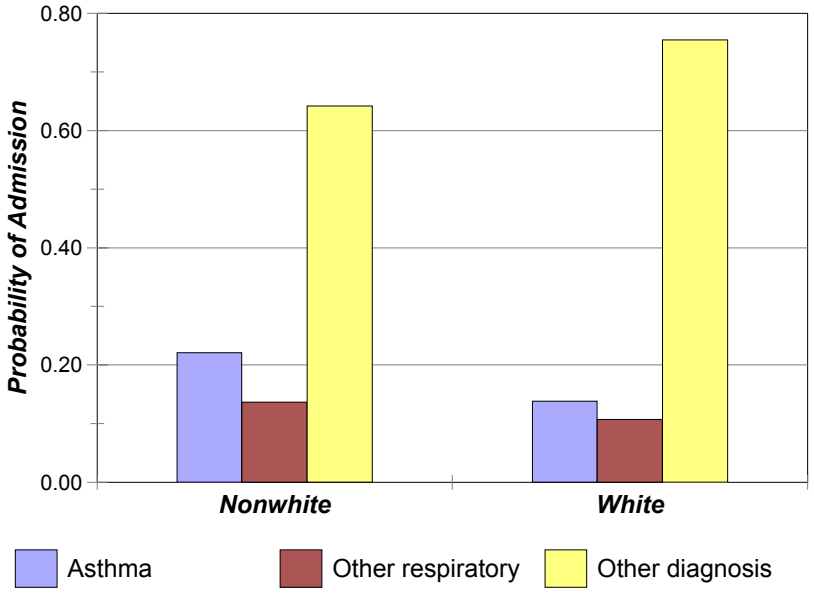

Figure 6-8: Race/ethnicity Effects on Admissions for Respiratory Illness

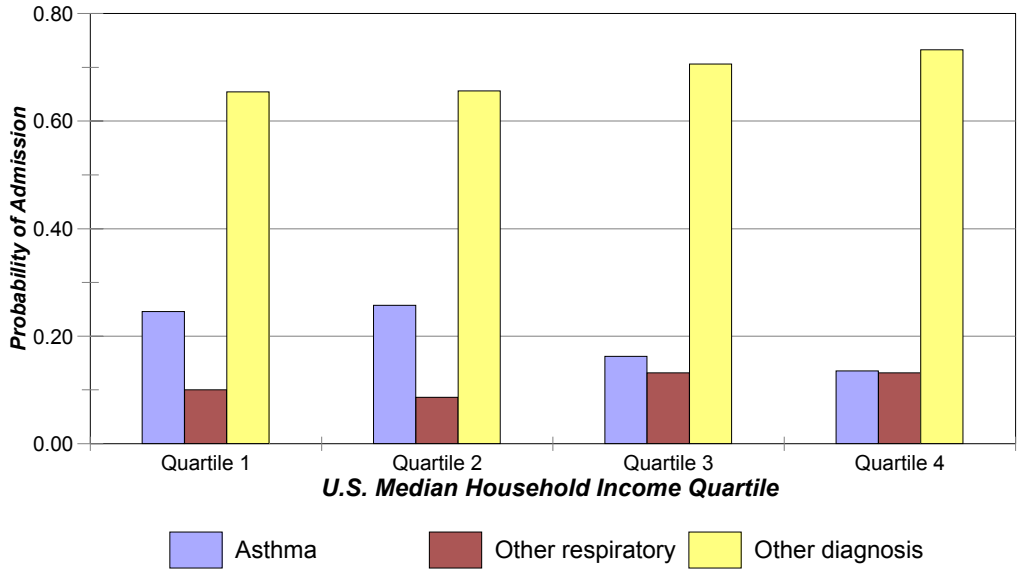

Figure 6-9: Median Household Income Percentile Effects on Admissions for Respiratory Illness

Figure 6-10 shows a small, statistically significant difference in hospital admissions for girls and boys. The Indianapolis data suggest that boys are more likely to be admitted for asthma and for other respiratory diseases than are girls, and this finding is consistent with other research.

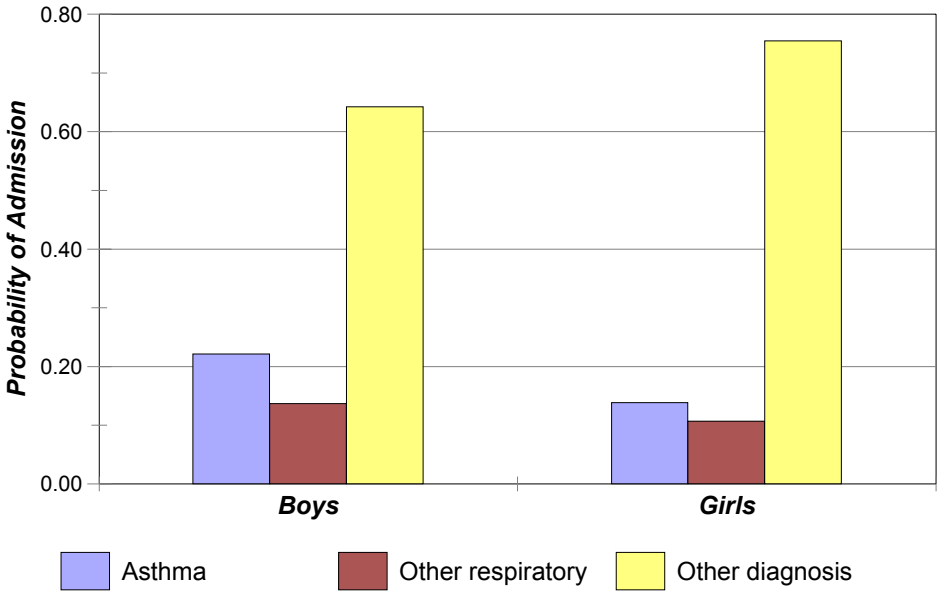

Figure 6-10: Differences between Boys and Girls on Admissions for Respiratory Illness

6.2.2 Multivariate Social Effects Models

This section provides the results of fitting alternative models of Race/ethnicity, Age, Income, and Sex, including models where Age and Income are assumed to be ordered categories. Table 6.9 suggests that there are complex relationships among Race/ethnicity, Age, Income, and Sex. The multivariate models reported in Table 6.9 are main effects models, meaning that the separate effects, whether ordered or unordered, are assumed to be multiplicative. Only one model -- that for Race and Median Household Income Percentile (unordered categories) meets the GOF test criterion ($p < 0.05$). The other models suggest the presence of interaction effects, which are more complex relationships between different levels of the predictor variables.

Table 6-9: Summary of Multivariate Social Effects Models Analyzed

Model	GOF Chi-square and Degrees of Freedom	Notes
Two Predictors		
Race/ethnicity x Age (unordered)	p = 0.0130, DF = 32	fails GOF test criterion
Race/ethnicity x Age (ordered)	p = 0.0001, DF = 62	fails GOF test criterion
Race x Sex	p = 0.0007, DF = 2	fails GOF test criterion
Race x Income (unordered)	NS	acceptable model
Race x Income (ordered)	p = 0.0759, DF = 10	fails GOF test criterion
Sex x Age (unordered)	p = 0.0001, DF = 32	fails GOF test criterion
Sex x Income (unordered)	p = 0.0102, DF = 6	fails GOF test criterion
Three Predictors		
Race/ethnicity x Sex x Age (unordered)	p = 0.0001, DF = 98	fails GOF test criterion
Race/ethnicity x Sex x Age (ordered)	p = 0.0001, DF = 128	fails GOF test criterion
Race/ethnicity x Sex x Income (unordered)	p = 0.0028, DF = 20	fails GOF test criterion
Race/ethnicity x Sex x Income (ordered)	p = 0.0022, DF = 24	fails GOF test criterion
Race/ethnicity x Age (unordered) x Income (unordered)	p = 0.0001, DF = 264	fails GOF test criterion
Race/ethnicity x Age (ordered) x Income (ordered)	p = 0.0001, DF = 264	fails GOF test criterion

Figure 6-11 reports the predicted probabilities of admission for asthma and other respiratory diseases by Race and U.S. Median Household Income Quartile, 1999. This figure shows distinct race and income effects on hospital admissions for asthma. Nonwhites are more likely than whites to be admitted for asthma, regardless of income level, and children from lower income households are most likely to be admitted for asthma than those children from the higher income households. Combining these two social effects, one finds that nonwhite children from households with the lowest incomes are most likely to be admitted to a metropolitan area hospital for asthma. Conversely, white children from the highest income households are least likely to be admitted for asthma. The estimated admission probability (percent) for asthma for nonwhite children from households in the 1st income quartile is 0.31 compared to 0.12 for white children from households in the 4th income quartile.

The estimated probabilities for other respiratory diagnoses also show statistically significant race and income effects. For these diagnoses nonwhites have a higher probability than whites to be admitted to an area hospital, but unlike asthma diagnoses, children from higher income households are more likely to be admitted than those from lower ones. Thus, nonwhite children from highest income quartile households are most likely to be admitted ($p = 0.14$), whereas white children from the lowest income quartile are least likely ($p = 0.08$) to be admitted.

The Indianapolis metropolitan area findings on social effects are consistent with other studies. Boys are more at risk from asthma than girls, and younger children, more so than older children. Race/ethnicity combine with Income to show statistically significant differences. Nonwhite children are more at risk than white children, and those living in the poorest households are similarly at greater risk.

The pattern for other respiratory diseases is different from asthma. Risks also decline with increased age, but at different rates, and there is a smaller boy-girl difference. The relationship between Race/ethnicity and Income and Other Respiratory diagnoses, however, are reversed. Though nonwhites are only slightly more at risk, children from higher income households are more likely to have an Other Respiratory disease diagnosis.

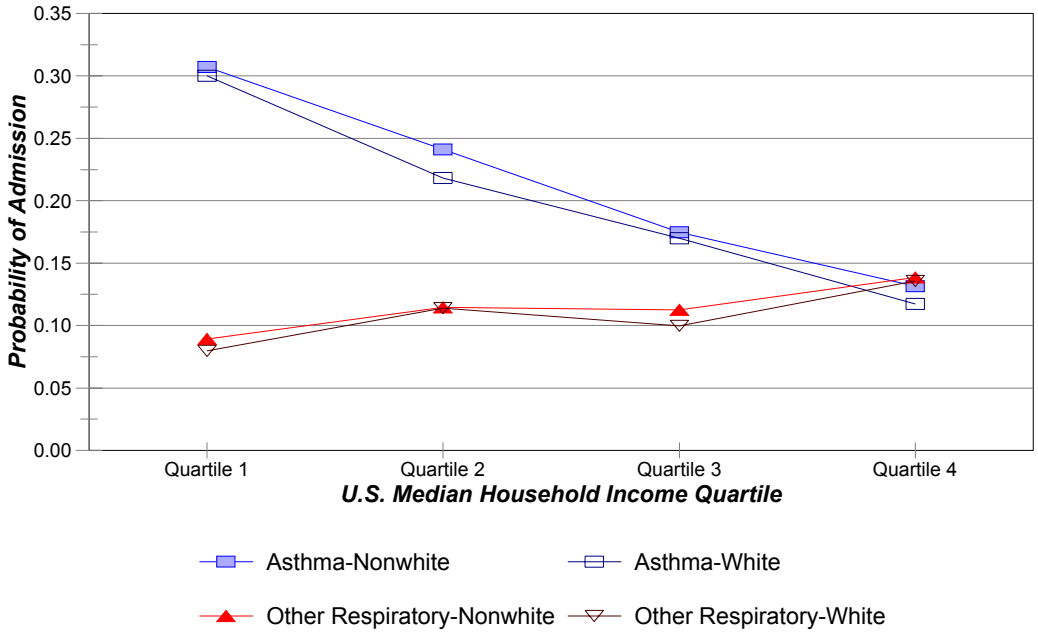

Figure 6-11: Predicted Probabilities of Admission for Asthma and Other Respiratory Diseases by Race and U.S. Median Household Income Quartile

6.3 Confounding Effects

This section examines the effects of two confounding variables, the day of the week when admitted and the source of admission, both of which are statistically related to the diagnoses. The Admission Source variable is classified into whether the patient first visited the emergency room or was an outpatient before being admitted (ER/Outpatient) or was routinely admitted or transferred to the hospital (Other).

Table 6-10 reports the results of three models fitted to the data -- a simple model for Day Admitted, a simple model for Admission Source, and a multivariate model combining Day Admitted and Admission Source. The simple models show that the both confounding variables explained a statistically significant amount of variation. The weekend days Saturday and Sunday as well as Mondays had higher probabilities for admission for asthma than the remaining days of the week. Admissions for other respiratory illnesses varied little during the week, but Fridays had a higher probability than the remaining days of the week. In sum, a more pronounced day effect is observed for asthma admissions than for other respiratory conditions.

The Admission Source variable showed that the ER/outpatient category had higher probabilities of admission for both asthma and other respiratory diseases than the routine admission (Other) category.

Table 6-10: Summary of Confounding Effects Models Analyzed

Model	GOF Chi-square and Degrees of Freedom	Effects Chi-square and Degrees of Freedom
Day of Week Admitted	saturated model; no GOF test	p = 0.0007, DF = 12
Admission Source	saturated model; no GOF test	p = 0.0001, DF = 2
Admission Source x Day of Week	p > 0.05; acceptable model	Source: p = 0.0001, DF = 2 Day: p = 0.1816, DF = 12

The multivariate model combining the effects of Admission Source and Day of the Week revealed a complex relationship between the two confounding variables and diagnosis. Figure 6-12 shows that both asthma and other respiratory illness diagnoses were more likely for patients admitted via the emergency room or as an outpatient than for patients with routine admissions (Other). For asthma diagnoses, patients admitted via the emergency room were more likely to arrive on Saturday (p = 0.27), Sunday (p = 0.25), or Monday (p = 0.25), but patients admitted routinely were more likely to come to the hospital during the middle of the week, and Wednesday was the most likely day of admission (p = 0.15).

For other respiratory diagnoses there was a higher probability of admission through the emergency room than through routine procedures. The probability of admission was slightly higher during the middle of the week, and Wednesday was the most likely day for admission for other respiratory illnesses, regardless of the admission source. For Wednesday, the probability of diagnosis for other respiratory diseases was 0.15 and 0.12 for emergency room and routine admissions, respectively.

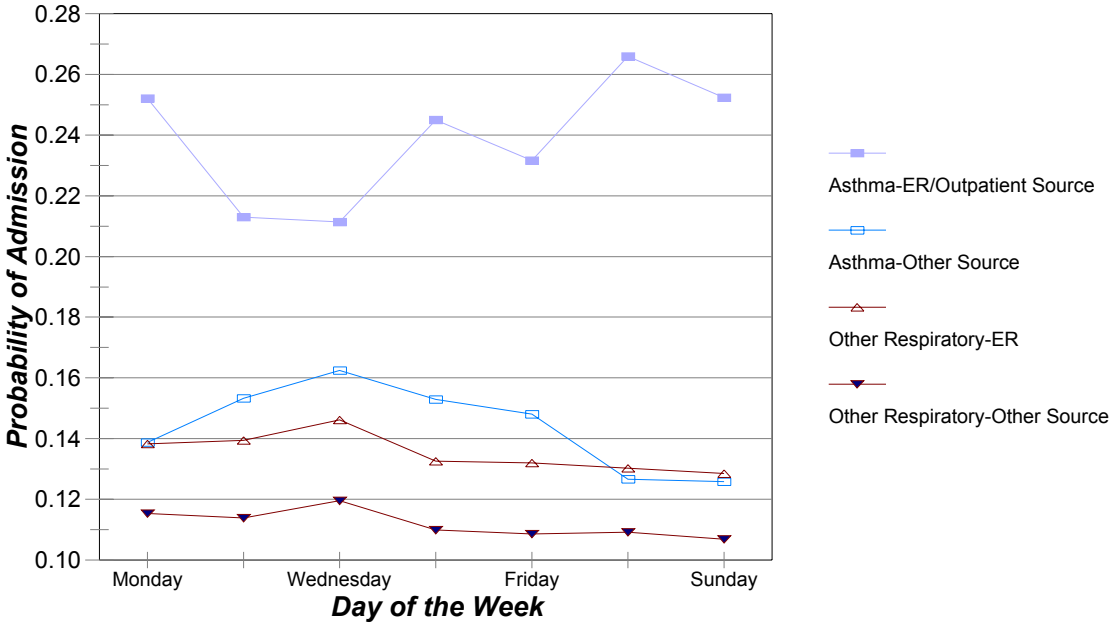

Figure 6-12: Effects of Admission Source and Day of the Week -- Admission for Asthma and Other Respiratory Diseases

7. CONCLUSION

The inherent nature of complex scientific studies, such as the Indianapolis Asthma Study, is that they answer some questions but often raise many others. It should be noted that all of the study's findings must be interpreted in the context of the strengths and limitations enumerated in Section 5. Within this context, the Indianapolis Asthma Study has provided findings consistent with the research literature on asthma -- namely, those regarding the positive effects of sulfur dioxide and nitrogen dioxide concentrations on asthma. These results should be viewed with caution because the concentrations of sulfur dioxide and nitrogen dioxide in the Indianapolis study were lacking in variability, low in comparison to the EPA standards, and low in comparison to other studies that reported statistically significant positive effects for asthma. It should be noted, however, that about 1/3 of the studies in the literature review, which reported statistically significant positive results for asthma and the oxides of nitrogen, had lower concentrations than the Indianapolis study. In the case of sulfur dioxide, the Indianapolis concentrations were lower than all of the studies that reported statistically significant results that could be compared. Among these, the Indianapolis concentrations were only slightly lower than about half of these studies. There is a possibility that the apparent correlations are the result of statistical coincidence, or alternatively, it is possible that there is a relation between these pollutants and hospital admissions for asthma in children at levels below the current EPA standards.

Additionally, the study found statistically significant relationships between age (negative), race/ethnicity (nonwhites greater than whites), household income (negative), and sex (boys greater than girls) on asthma. These results suggest that as children age they are better able to manage their disease, or alternatively, asthmatic attacks become less severe. In addition, the results for race/ethnicity and income suggest that a greater need and opportunities may exist for intervention programs among nonwhites and lower income levels in the Indianapolis area.

The major anomaly in the study is the finding of a statistically significant negative association between ozone and asthma. The research literature on ozone and asthma reports mixed results. The plurality of studies reviewed show a statistically significant relationship, and among 14 studies reporting statistically significant associations between ozone and asthma, 11 reported positive findings. Though the Indianapolis study found a statistically significant relationship, it adds to the uncertainty about the true relationship between ozone and asthma for children. Although the Indianapolis data was marked by relatively little variability in the concentrations and the ozone levels were relatively low in comparison to other levels in the state and in neighboring, the Indianapolis concentrations of ozone were higher than the studies that reported a negative association with asthma and higher than all but three of the studies that reported a positive association with asthma in those cases where comparisons could be made. More work is needed to verify this relationship and examine this outcome.

This research project also contributed findings to areas of the research literature on temperature, relative humidity and dew point, where information is sparse. In this study, relative humidity, temperature, and dew point have statistically significant negative relationships with asthma. Potential interactions among the meteorological variables and the environmental variables should be examined in future work.

The Indianapolis Asthma Study broke new ground by examining in detail the effects of environmental and social conditions on other respiratory diseases. There were no statistically significant findings for any of the six environmental variables on the Other Respiratory Disease category.

The Indianapolis study also breaks new methodological ground in several important ways. One is the use of multinomial logit analysis and estimates of within group variations based on individual-level counts, such as race/ethnicity, age, sex, income, and exposures levels, to environmental conditions. All but two of the asthma studies reported in Appendix A utilized variations and combinations of regression, correlation, and time series analysis of aggregated daily counts. This research study also made use of GIS software to link the closest air quality monitor to the individual subject's address (ZIP code). Additionally, this study used individual estimates of U.S. Median Household Income based on ZIP code rather than using metropolitan area or county estimates of income. Finally, the Indianapolis study conducted a pilot study of misclassification errors in the diagnosis of asthma that produced evidence of an undercount of asthma cases. The net effect of these methodological contributions is that the study provides more information about the variations in conditions affecting asthmatic children.

This summary of the findings points the way toward the "next steps" for the Central Indiana Asthma Research Project to further advance the scientific understanding of how environmental and social conditions affect asthma and other respiratory diseases in Indiana and elsewhere. The following sections discuss the possible expansion of this study and the need for methodological research to improve the study design.

7.1 Future Studies

Overall, more work needs to be done to elucidate the relationship between childhood asthma and exposure to environmental conditions. The authors of this study suggest two separate studies that that build on the Indianapolis study and continue to expand both the breadth and depth of the knowledge of how environmental and social conditions affect asthma in Indiana.

Comparative Study of Metropolitan Areas: From an environmental quality viewpoint, the Indianapolis metropolitan area is a better environment on most air quality measures for children than other metropolitan areas in Indiana. The children studied here, with few exceptions, did not experience the more extreme levels of pollution reported in some other studies or found elsewhere in Indiana. A future study should add other Indiana metropolitan areas for comparison -- possibly, Gary, Evansville, Fort Wayne, and Terre Haute. A review of the air quality in these metropolitan areas along with a determination of the availability of comparable hospital records to those used in this study is necessary before undertaking this comparative study. A comparative study may demonstrate that higher ozone levels are positively associated with health outcomes and confirm the relationship for other pollutants.

City of Indianapolis Study with Outpatient Data: Where the comparative study would add breadth to the research findings, a research analysis incorporating outpatient/emergency room data would add considerable depth. The original study design of the Indianapolis Asthma Study called for the inclusion of emergency room and outpatient hospital records, information only available directly from area hospitals. The considerable burden placed on hospital staff to produce a data file of admission records delayed this project nearly 12 months and ultimately led to the use only of inpatient data provided by the assistance of the Indiana Hospital and Health Association and its member institutions. The analysis of data provided directly by one area hospital suggests that substantial improvements in the understanding of air quality and asthma would result from a study of inpatient and outpatient data provided by hospitals in Marion County (City of Indianapolis). Expanding the health data to include records from private physicians would be an additional improvement, but one that would be considerably more time consuming and costly to incorporate.

7.2 Methodological Research

Neither of the above studies should be undertaken without incorporating some methodological improvements listed below.

Add Particulate Data: Though the original study design intended to use the PM10 and PM2.5 data collected for the metropolitan area, the authors eliminated it from this study because of missing data and the sampling frequency. The review of the research literature further enforces the conclusion that such information should be included to provide a complete picture of air quality effects on asthma and respiratory conditions in children. Further work is needed to explore methodologies to handle missing data and estimate daily particulate levels, or alternatively, methodologies to analyze a subset of the data so particulate data can be included in the analysis.

Add Pollen and Spore Data: The original study design intended to incorporate daily counts of pollen and fungal spores into the analysis because these measurements have been identified as potentially important variables in some research studies. Measurements of pollen and fungal spores were available from one site in Indianapolis, but the missing data precluded the use of these variables in the study. Further work is needed to explore methodologies to handle data gaps, or alternatively, methodologies to analyze a subset of the data so pollen and spores can be included in the analysis.

Review the Classification of Other Respiratory Diseases: The methodology to measure asthma used in this study is well-established in the research literature. Future studies using the Other Respiratory disease category require further methodological research to establish the validity and reliability of the classification procedures.

Review the Base Category: The multinomial logit analysis used in this study had a base category containing all other diagnoses excluding asthma and other respiratory diseases. In other words, it was the complement of the first two categories. The choice of a base category involves the consideration of what should be the "control" group in a non-experimental study. This pseudo control group should have the property of having no "treatment" effects. Further research is needed to determine whether the choice of another base category would substantially alter the findings reported in this study.

Adjust for Correlated Data: In this report, hospital admissions were assumed to be independent; however, children could have had more than one admission, which was the product of a single asthmatic episode, throughout the study. In future studies, methods should be explored for making adjustments for hospitals admissions and other potentially correlated data in Multinomial Logit Models.

Analyze Additional Metrics of Environmental Measures: In this report, the analysis focused on daily mean and moving averages of environmental measures to model exposures. Future work should consider other measures, especially those that isolate ozone episodes.

Incorporation of some or all of these six methodological improvements is a necessary part of any future studies of the effects of environmental and social conditions on asthma among children in Indiana.

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9. Technical Appendixes

Table A.1

Summary of Epidemiologic Studies of Air Pollution and Health Care

for Asthma and Other Respiratory Conditions in Children—Environmental Measures

Author (Year of Publication)	Location of Study	Period of Study[1]	Pollutants Included in the Statistical Analysis[2]					Meteorological Parameters[3]	Comments
			O3	SO2	NO2	Particles	Other		
A. Ozone Significant1									
Bates and others (1990)	Vancouver	1984-86 (CY, S, W)	X	X	X	SO4, COH		T (daily maximum)	O3, SO2, NO2 - 11 monitoring sites; COH - 1 monitor; SO4 - 2 monitors; PM dichotomous monitor - 1 site 1 meteorology station
Pönkã (1991)	Helsinki	1987-89 (CY)	X	X	X (& NO)	TSP	CO	✓ T (minimum & mean daily), ✓WS ☒ RH	O3 - 1 UV monitor; SO2 - 4 coulometric monitors; NO2 - 2 chemiluminescence monitors; particles - 6 high volume monitors; CO - 2 NDIR monitors; concentrations averaged over monitoring sites 1 meteorology station
Burnett and others (1994)	Ontario	1983-88 (CY, S)	X			SO4		✓ T (mean & maximum), ✓BP ☒ RH	O3 - 22 stations; SO4 - 9 stations; measurements linked to hospitals by region 10 meteorology stations
White and others (1994)	Atlanta	1990 (S)	X	X		PM10, visibility	pollen	✓ T, ✓DP	O3 - 2 monitors; SO2-- 2 monitors; particles - ? PM10 monitors; visibility also used as surrogate for PM and missing days were interpolated; pollen - 1 monitor; concentrations averaged over monitoring sites 1 meteorology station
Romieu and	Mexico	1990 (1st	X	X	X	TSP		✓ T	All pollutant parameters - 1 monitor; 18/24

others (1995)	City	6 mos)							hrs required for completeness; TSP analyzed as subset 1 meteorology station
Buchdahl and others (1996)	London	1992-93 (CY)	X	X	X			✓ T, ✓WS	All pollution parameters - 1 monitor (differential absorption spectroscopy) 1 meteorology station
Pönkã & Virtanen (1996)	Helsinki	1987-89 (CY)	X	X	X	TSP		✓ T ☒ RH	O3 - 1 UV monitor; SO2 - 4 coulometric monitors; NO2 - 2 chemiluminescence monitors; TSP - 6 high volume samplers (4 sampled every 2nd day and 2 every 3rd day); concentrations averaged over all sites when more than 1 site was available 1 meteorology station
Medina and others (1997)	Paris	1991-95 (CY)	X	X	X	BS, PM13		✓ T ☒ DP	O3 - 5 UV monitors; SO2 - 9 UV monitors; NO2 - 8 chemiluminescence monitors; BS - 12 reflectometers; PM13 - 4 β radiometry monitors; concentrations averaged over monitoring sites 1 meteorology station
Anderson and others (1998)	London	1987-92 (S)	X	X	X	BS	pollen, spores	T (warm/cool), ☒ RH	O3 - 1 UV monitor; SO2 - 4 bubbler monitors; NO2 - 2 chemiluminescence monitors; particles - 4 BS monitors; pollen - 1 volumetric spore trap; concentrations averaged over monitoring sites when more than 1 site was available 1 meteorology station
Chew and others (1999)	Singapore	1990-94 (CY)	X	X	X	TSP		WS, solar radiation ☒ T & ☒ RH (minimum & maximum)	Information on environmental monitoring methods and number of stations not provided
Fauroux and others (2000)	Paris	1998 (CY)	X	X	X	BS	pollen - 2 sites	☒ T, ☒ RH	O3 - 5 UV monitors; SO2 - 11 UV monitors; NO2 - 8 chemiluminescence monitors; BS - 15 reflectometers; PM13 - 4 β radiometry monitors; concentrations

									averaged over monitoring sites 1 meteorology station
Tolbert and others (2000)	Atlanta	1993-95 (S)	X		X (NO X)	PM10	pollen, mold	T, RH	10 O3 monitors; 1 NOx monitor; 1 PM10 monitor with data collected 5-6 days/wk; 1 pollen/mold monitor with data collected 5 days/wk; used kriging in GIS procedure to interpolate O3 concentrations from available data; O3 linked to zip code centroid number of meteorology stations not provided
B. Ozone Not Signficant2									
Bates & Sizto (1983)	Southern Ontario	1974-78 (S=Jul & Aug; W=Jan & Feb)	X	X	X	COH		T	All pollutants - 15 sites; concentrations averaged over all monitoring sites; 0-2 day lags used 2 meteorology stations - average of the 2 stations used
Bates & Sizto (1987)	Southern Ontario	1974-83 (CY, S, W)	X	X	X	SO4, COH		T , RH	All pollutants - 16 sites; O3 & SO2 - 1 additional site; SO4 by filtration and chromatographic analysis; adjustment to SO4 data for glass fiber filter 1 meteorology station
Rennick & Jarman (1992)`	Melbourn e	1989 (CY)	X			API	SAD; SED		7 monitoring sites; API - airborne particulate index; SAD – smog alert days and SED - smog episode days; no difference between summer and winter analysis; it is not known if concentrations averaged over monitoring sites
Tseng and others (1992)	Hong Kong	1983-89 (CY)	X	X	X	TSP, RSP	NOx		Up to six different locations for O3, SO2, NO2, TSP and RSP (respiratory suspended particles); monthly means based on daily averages over all monitoring sites were used for analysis

Schwartz and others (1993)	Seattle	1989-90 (CY)	X	X		PM10; βsp; PM2.5		T, RH	O3 - 1 monitor for 5 mos.; SO2 - 1 industrial monitor; PM10 - 3 monitors; PM2.5 - 2 monitors; βsp - 1 monitor; concentrations averaged over all monitoring sites 1 meteorology station
Burnett and others (1995)	Ontario	1983-88 (CY)	X	X	X	SO4,		BP, ☒ T (minimum & maximum), ☒ RH	O3 - 22 sites; SO2 & NO2 -5 sites; SO4 - 9 monitors; SO4 results adjusted for artifact on glass fiber filters; measurements linked to hospitals by region; 1 set of monitors for each region 10 meteorology stations
Stieb and others (1996)	St. John, New Brunswick	1984-92 (S)	X	X	X	TSP	sulfate	T, RH, humidex, DP	O3 - UV monitors; SO2 - pulsed fluorescence; NO2 - chemiluminescence monitors; TSP - high volume sampler; sulfate from TSP filters; authors did not report number of monitoring sites, but concentrations averaged over all sites when more than 1 site was available number of meteorology stations not reported
Sunyer and others (1997)	Barcelona, Helsinki, Paris, and London	1986-92 (CY)	X	X	X	BS	influenza; soybean epidemic in Barcelona	☒ T, ☒ RH	Barcelona - 3 sites; London - 4 sites; Paris - 4 sites; Helsinki - 8 sites; details on monitors not provided; referenced to original papers number of meteorology stations not reported
Morgan and others (1998)	Sydney	1990-94 (CY)	X		X	PM2.5		T & DP (daily mean)	3 sites in 1990 and 14 sites in 1994; PM by nephelometer, equivalent to 2.5 microns RH data included, but not in statistical analysis number of meteorology stations not reported

Rosas and others (1998)	Mexico City	1991 (CY, wet, dry	X	X	X	TSP	pollen, spores	T (daily minimum & maximum), RH (daily average), rainfall (daily)	Number of monitoring sites not reported
Atkinson and others (1999)	London	1992-94 (CY)	X	X	X	PM10	CO, pollen	☒ T, ☒ RH	8 sites; O3 - 2 monitors; SO2 - 1 5 monitors; NO2 - 2 monitors; PM10 - 1 monitor; CO - 3 monitors; concentrations averaged over monitoring sites
C. Ozone Significant, but Negative3									
Holmén and others (1997)	Halmstad, Sweden	1990-93 (CY)	X	X	X		toluene, pollen	T, RH, WS, WD	1 site - differential optical absorption spectroscopy for pollutants 1 meteorology station
Anderson and others (1998)	London	1987-92 (S)	X	X	X	BS	pollen, spores	T (warm/cool), ☒ RH	O3 - 1 UV monitor; SO2 - 4 bubbler monitors; NO2 - 2 chemiluminescence monitors; particles - 4 BS monitors; pollen - 1 volumetric spore trap; concentrations averaged over monitoring sites when more than 1 site was available 1 meteorology station
Garty and others (1998)	Israel	1993 (CY)	X	X	X	PM	pollen, spores	BP (minimum & maximum) ☒ T & ☒ RH (minimum & maximum)	O3 - 1 UV monitor; SO2 - 1 pulsed fluorescence monitor; NO2 - 1 chemiluminescence monitor; particles - 1 ambient particle monitor 1 meteorology station

[1] CY - calendar year; S - summer; W - winter

[2] An "X" indicates that the pollutant was measured and included in the statistical analysis. These pollutants are linked to findings in Table A.2. A blank box means that the variable was not measured. Additional symbols include ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), nitrogen oxide (NO), nitrogen oxides (NO_x), particulate matter (PM), particulate matter < 2.5 microns ($PM_{2.5}$), particulate matter < 10 microns (PM_{10}), particulate matter < 13 microns (PM_{13}), black smoke (BS), respirable particulates (RSP), coefficient of haze (COH), sulfates (SO_4), and carbon monoxide (CO).

[3] A listed parameter that does not have a symbol in front of it means that the parameter was included in the study and in the statistical analysis. If the parameter has a ✓ in front of it, the parameter was included in the statistical analysis as an independent variable. A ☒ in front of the parameter means the parameter was included in the study but not in the statistical analysis. Additional symbols include temperature (T), relative humidity (RH), dew point (DP), wind speed (WS), wind direction (WD), and barometric pressure (BP).

Table A.2

Summary of Epidemiologic Studies of Air Pollution and

Health Care for Asthma and Other Respiratory Conditions in Children—Findings

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
A. Ozone Significant[1]									
Bates and others (1990)	Vancouver	1984-86 (CY, S, W)	✓Asthma hospital admission; other respiratory hospital admissions	Regression, correlation	SO_4 in summer for asthma; SO_2 in winter for other respiratory O_3 and T in summer & T in winter for total respiratory all for ages 1-14 yrs	SO_2 and SO_4 in summer for asthma; SO_2, NO_2, and SO_4 in summer & SO_2 in winter for other respiratory O_3 and T in summer & winter for total respiratory all for ages 15-60 yrs)	SO_4 in summer & SO_2 and SO_4 in winter for asthma; SO_4 in summer & SO_2, NO_2, and SO_4 in winter for other respiratory. O_3, T in summer & SO_2 in winter for total respiratory all for ages 61+	—	9 hospitals included; same day, 1-day and 2-day lags important; in the age group 0-14 yrs, SO_4 was not significant in winter
Pönkã (1991)	Helsinki	1987-89 (CY)	✓Asthma hospital admission; emergency ward admission (EW)	Regression, correlation; Time series	O_3, NO for EW admission	NO_2, NO SO_2, CO, TSP, (T), cold for EW admission	NO_2, NO SO_2, cold for EW admission; CO for asthma	NO, CO, O_3 for EW admission T?	Pollutants explained about 14% in RA; 1 & 2 day lag important; log transform increased explanatory power of model

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
Burnett and others (1994)	Ontario	1983-88 (CY, S)	✓Asthma, COPD, and infection hospital admission	Time series	O_3, SO_4 for ages 0-1 yrs T?	O_3. SO_4 for ages 2-34 yrs & 35-64 yrs T?	T?	O_3, SO_4 T?	168 acute care hospitals included; 0 to 3-day lags important; daily 1-hr ozone a stronger predictor than daily average sulfate concentration; authors conclude that infants were more sensitive than adults
White and others (1994)	Atlanta	1990 (S)	✓Asthma or reactive airway disease emergency room (ER) visits	Non-parametric rank analysis	O_3, for ages 1-16 yrs (DP)	—	—	—	Indigent, predominantly black population; O_3 levels > 0.11 ppm important; 1 day lag
Romieu and others (1995)	Mexico City	1990 (1[s] 6 months)	✓Asthma ER visits	Poisson regression	O_3, SO_2 for ages < 16 yrs	—	—	—	O_3 results significant for lags of 0-2 day; model predicted 50 ppb increase in 1-hr O_3 would lead to 43% increase in emergency room visits the following day
Buchdahl and others (1996)	London	1992-1993 (CY)	✓Acute wheezy episode ER admission	Poisson regression; Non-parametric rank analysis	O_3, SO_2, (T), (WS)	—	—	—	Non-linear U-shaped relation for O_3; weaker log-linear relation for SO_2
Pönkã & Virtanen (1996)	Helsinki	1987-89 (CY)	✓Asthma hospital admission	Regression, correlation; Time series	O_3, (T)	SO_2, (T)	SO_2 T?	—	Authors report modeling problematic because O_3 also significantly associated with digestive tract disorders (the control)
Medina and others (1997)	Paris	1991-95 (CY)	✓Asthma house calls	Poisson regression	O_3,* NO_2, SO_2, BS, PM_{13} T?	Similar to findings for ages 0-14 yrs T?	—	T, and other findings similar to those for ages 0-14 yrs	*O_3 & asthma showed interaction with temp; effect only present when minimum temperature in summer on the previous day was > 10ºC; 0 day lag for O_3 in children; 0-3 day lag for other parameters

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
Anderson and others (1998)	London	1987-92 (CY, S, W)	✓Asthma hospital admission	Poisson regression	NO_2, SO_2 for CY; O_3 & NO_2 in summer (O_3) & NO_2 in winter T?	O_3 for CY & in summer T?	NO_2, BS for CY; NO_2, SO_2, BS in winter T?	NO_2, SO_2, BS for CY; O_3, SO_2 for summer (O_3), NO_2, SO_2, BS in winter T?	Negative association for O_3 in winter; no consistent pattern for pollen; cumulative lags up to 3 days showed stronger and more significant effects than single day lags
Chew and others (1999)	Singapore	1990-94 (CY)	Asthma hospital admissions	Time series	O_3, SO_2, TSP, NO_2 for ANOVA SO_2, NO_2, TSP for regression all for ages 3-11 yrs	O_3 for ANOVA all for ages 12-21 yrs	—	—	0-2-day lags important; < 3yrs not used because of problems with diagnosis of asthma; O_3, SO_2, TSP, NO_2 not significant for 13-21 year olds; after adjustment for meteorological and temporal variables, only SO_2 and TSP significant for 1 day lag
Fauroux and others (2000)	Paris	1998 (CY)	✓Asthma ER visits	Poisson regression	O_3, for ages 1-15 yrs	—	—	—	O_3 significant with 1-day lag after adjusting for meteorology, pollen, influenza, time-related variables
Tolbert and others (2000)	Atlanta	1993-95 (S)	Asthma ER visits	Logistic regression	O_3, PM_{10} modeled singly or with T T in multiple regression models	—	—	—	1-2-day lags important in GEE; for logistic regression males, African-Americans and the poor had increased risk of being an asthma case; data suggest exposure response for O_3 and PM_{10}
B. Ozone Not Significant[2]									

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
Bates & Sizto (1983)	Southern Ontario	1974-78 (S=Jul & Aug; W=Jan & Feb)	✓Asthma & respiratory hospital admissions	Regression, correlation		—	—	O_3 in summer for asthma O_3, SO_2, T in winter & T in summer for respiratory admissions T in summer & SO_2, O_3, NO_2, and T in winter for total hospital admissions	
Bates & Sizto (1987)	Southern Ontario	1974-83 (CY, S=Jul & Aug; W=Jan & Feb)	✓Asthma & respiratory hospital admissions	Regression, correlation	(NO_2), T in winter for asthma	—	—	T in winter & O_3, SO_2, (SO_4) in summer for asthma; SO_2, O_3, (SO_4) in winter for other respiratory conditions	Same day and 1-day lag important; in age group 0-14 yrs, T was not significant in summer for asthma
Rennick & Jarman (1992)`	Melbourne	1989 (CY)	☒ Asthma ER visit	Regression, correlation	API > threshold for ages >2 yrs	—	—	—	No association with O_3 or smog variables; O_3 threshold was 0.09 ppm in this study
Tseng and others (1992)	Hong Kong	1983-89 (CY)	⊕ Asthma hospital admissions	Regression, correlation	TSP for ages 1-4 yrs; (SO_2) for ages 5-14 yrs	—	—	—	Quarterly mean concentrations analyzed; authors conclude that young children are vulnerable to the adverse effects of pollution; no significant effects for 0 to 1 year age group
Schwartz and others (1993)	Seattle	1989-90 (CY)	✓Asthma ER visit	Poisson regression	PM_{10} for ages < 5 yrs and 6-20 yrs T?	PM_{10} for ages 21-65 T?	—	PM_{10} & β_{sp} for ages < 65 yrs T?	4-day lag of PM_{10} better predictor; daily PM_{10} low and never exceeded 70% of NAAQS; analysis by age group not included for O_3 or SO_2

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
Burnett and others (1995)	Ontario	1983-88 (CY)	✓Respiratory (including asthma & cardiac) hospital admission	Time series	SO_4	SO_4	SO_4	SO_4	SO_4 association positive for cardiac and respiratory hospital admissions in all age groups after adjustment for temp, O_3, and season; specific results not given for O_3; 1-day lag for SO_4 was important
Stieb and others (1996)	St. John, New Brunswick	1984-92 (S)	✓Asthma ER visits	Regression, correlation	T?, RH?, DP?	O_3 for ages > 15 yrs T?, RH?, DP?	—	O_3 T, RH, DP	Daily average and daily 1-hr max NS for O_3 in children; lags of 0-3 days used
Sunyer and others (1997)	Barcelona, Helsinki, Paris, and London	1986-92 (CY)	✓Asthma ER visits	Poisson regression (meta-analysis)	SO_2, NO_2 in meta analysis (Helsinki, Paris, & London)	NO_2 in meta analysis (all 4 cities)	—	—	Outcome variable is not strictly the same among all cities; 24-hr ave for SO_2 and 24-hr ave and 0-3-day lags for NO_2 were significant in children for all cities combined; in 2 pollutant models only SO_2 significant for children and only NO_2 significant for adults
Morgan and others (1998)	Sydney	1990-94 (CY)	✓Asthma, hospital admissions for COPD & heart disease	Regression, correlation; Poisson regression	NO_2 for asthma for single & multiple pollutant model T?, RH? all for ages 1-14 years	NO_2 for heart disease T?, RH? all for ages 0-65 yrs	PM & NO_2 for heart disease T?, DP?	PM & NO_2 for heart disease T, DP	1-hour max NO_2 was significant for childhood asthma; no variables significant for age group 15-69 yrs for asthma
Rosas and others (1998)	Mexico City	1991 (CY, wet/S, dry/W)	✓Asthma ER visits	Poisson regression	T, grass pollen & fungal spores for wet and dry seasons	RH, grass pollen for we and dry seasons all for ages 16-59 yrs	T?, RH? all for ages <59 yrs	—	0 to 2-day lags used for environmental data

First Author (Year of Publication)	Location of Study	Period of Study[1]	Outcome Measure[2]	Principal Statistical Analysis Method	Significant Findings by Age[3, 4]				Comments
					0-14 yrs	15-64 yrs	65+ yrs	All Ages	
Atkinson and others (1999)	London	1992-94 (CY)	✓Asthma, other respiratory ER visits	Poisson regression; Time series	SO_2, NO_2, PM_{10} for asthma; SO_2, CO, PM_{10}, BS for all respiratory complaints	NO_2, CO, PM_{10}, BS for asthma; PM_{10}, BS for all respiratory complaints	NO_2, O_3, SO_2, CO, BS for all respiratory complaints	NO_2, SO_2, CO, PM_{10} for asthma; SO_2 & PM_{10} for all respiratory complaints	Results for asthma and children strongest for SO_2 & NO_2; 1-day lag important for SO_2, NO_2 and asthma in children PM_{10}; 2 pollutant models reduced magnitude and effect of single associations reported in this study
C. Ozone Significant, but Negative[3]									
Holmén and others (1997)	Halmstad, Sweden	1990-93 (CY)	✓Asthma ER visits	Regression, correlation	NO_2, (T) for t-test NO_2, (T), (O_3) for ANOVA	O_3, (NO_2), toluene for t-test T, O_3, (NO_2), toluene for ANOVA	—	—	Looked at differences between days with low number of asthma visits and days with high number of asthma visits
Anderson and others (1998)	London	1987-92 (CY, S, W)	✓Asthma hospital admission	Poisson regression	NO_2, SO_2 for CY; O_3 & NO_2 in summer (O_3) & NO_2 in winter T?	O_3 for CY & in summer T?	NO_2, BS for CY; NO_2, SO_2, BS in winter T?	NO_2, SO_2, BS for CY; O_3, SO_2 for summer (O_3), NO_2, SO_2, BS in winter T?	Negative association for O_3 in winter; no consistent pattern for pollen; cumulative lags up to 3 days showed stronger and more significant effects than single day lags
Garty and others (1998)	Israel	1993 (CY)	✓Asthma ER visits	Regression, correlation	NO_x, SO_2, barometric pressure, (O_3) all for ages 1-18 yrs	—	—	—	

[1] CY - calendar year; S - summer; W - winter

[2] A ✓ in this column means that the outcome measure was in the form of a daily frequency (count). A ☒ means that the outcome measure was a weekly frequency (count) and a ⊕ means that the outcome measure was an age-specific rate.

[3] See Table A.1 to determine which pollutant and meteorological variables were included in the statistical analysis. Variables that were not significant do not appear in this column. Variables from Table A.1 that were significant are listed in this column. If the direction of the significant relationship is positive, the variable appears without a parenthesis. A significant but negative relationship is identified by a parenthesis. A "?" means that there was some uncertainty, either in the text or data, about the association or it was not possible to determine if an association existed. The symbol, "—," means there were no data for that age group for any of the variables. A box that does not have an entry means

that none of the variables included in the statistical analysis were significant. Additional symbols include ozone (O_3), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), nitrogen oxide (NO), nitrogen oxides (NO_x), particulate matter (PM), particulate matter < 10 microns (PM_{10}), particulate matter < 13 microns (PM_{13}), black smoke (BS), sulfates (SO_4), carbon monoxide (CO), temperature (T), relative humidity (RH), dew point (DP), and wind speed (WS).

[4] Departures from age grouping given in each column heading are included, as appropriate, in the column.

APPENDIX B

Summary of Air Quality Monitoring Site Locations, Methods, and Percent Missing Data for the Central Indiana Study Area[1]

Parameter and Site ID	Site Address	Land Use	Location Setting	Method	Percent Missing Data2
Ozone					
18-109-0005	135 S. Chestnut, Monrovia High School, Monrovia	Agricultural	Rural	UV Photometry	2.7
18-057-1001	1775 Field Dr., School Bus Barn, Noblesville	Residential	Suburban	UV Photometry	1.1
18-095-0010	East Elementary School, 893 E. U.S. 36, Pendleton	Agricultural	Rural	UV Photometry	0.2
18-059-0003	714 E. Broadway, Municipal Building, Fortville	Commercial	Suburban	UV Photometry	4.4
18-081-0002	200 W. Pearl St., Trafalgar	Agricultural	Rural	UV Photometry	3.5
18-097-0042	8327 Mann Rd., Indianapolis	Agricultural	Rural	UV Photometry	0.9
18-097-0057	1321 South Harding, Indianapolis	Residential	Urban, Center City	UV Photometry	2.3
18-097-0050	Fort Harrison State Park, Indianapolis			UV Photometry	3.3
18-097-0073	Naval Avionics Center, 6125 E. 16th Street, Indianapolis	Residential	Urban, Center City	UV Photometry	0.6
Nitrogen Dioxide					
18-097-0073	Naval Avionics Center, 6125 E. 16th St., Indianapolis	Residential	Urban, Center City	Chemiluminescent	0.9
Sulfur Dioxide					
18-097-0042	8327 Mann Road, Indianapolis	Agricultural	Rural	Pulsed Fluorescent	0.2
18-097-0057	1321 South Harding, Indianapolis	Residential	Urban, Center City	Pulsed Fluorescent	0.9
18-097-0072	50 North Illinois St., Indianapolis	Commercial	Urban, Center City	Pulsed Fluorescent	0.2
18-097-0073	Naval Avionics Center, 6125 E. 16th St., Indianapolis	Residential	Urban, Center City	Pulsed Fluorescent (1997) & UV Stimulated Fluorescent (1997-1999)	0.9

[1]For the period May 1 – September 30, 1997 – 1999

[2]Missing data reported for daily means; percent of values missing from each site's total potential values (459 days during the period of study).

APPENDIX C

Indianapolis Asthma Study Codebook Field Definitions with Recoded Values
(June 2001)

FIELD NAME	DESCRIPTION	TYPE	VALUES	DATA SOURCE
HOSPID	Hospital ID	Num	3, 87, etc.	IHHA
HOSPIDC	Hospital Name	Char 30	2 Hancock Mem, Greenfield 24 St. Vincent Mercy, Elwood 3 St Johns, Anderson 72 Morgan Co Mem, Martinsville 87 Community-Anderson, Anderson 99 Johnson Mem, Franklin 102 Major Hosp, Shelbyville 124 Riverview, Noblesville 137 Community-South, Indpls 138 Community-East, Indpls 139 Community-North, Indpls	Recoded numeric values from list provided by IHHA
ADMTSORC	Admission source code	Num	1-4	IHHA
ADMTSRCC	Source of admission labels	Char 15	1..... Routine 2..... Transfer 3..... Outpatient/ER 4.....Other	Recoded numeric values from list provided by IHHA
ADMTDATE	Date of admission	Date	05/14/97, etc.	IHHA
ADMTYEAR	Year of admission	Num	1997, etc.	Derived from ADMTDATE
ADMTMNTH	Month of admission	Num	5, etc.	Derived from ADMTDATE
ADMTDAY	Weekday of admission	Num	1-7	Derived from ADMTDATE
ADMTDAYC	Weekday of admission labels	Char 9	1..... Sunday 2.....Monday 3.....Tuesday 4.....Wednesday 5.....Thursday 6.....Friday 7..... Saturday	Derived from ADMTDATE
DSCHDATE	Date of discharge	Date	05/16/1997, etc.	IHHA
STAY	Number of days of stay in hospital	Num	2, etc.	IHHA
BRTHDATE	Date of birth	Date	12/07/95, etc.	IHHA
AGEYR	Age in years	Num	1, etc.	Derived from ADMTDATE and BRTHDATE
AGEMO	Age in months	Num	17, etc.	Derived from ADMTDATE and BRTHDATE
RACE	Race of patient	Num	1, 2, 8	IHHA; values 3-Minority and 4-Other converted to 8
RACEC	Race of patient labels	Char 5	1..... White 2.....Black 8.....Other	Recoded numeric values from list provided by IHHA
RACE2	Recoding of RACE	Char 8	1..... White Other.....Nonwhite	Derived from RACE
SEX	Gender of patient	Num	1, 2	IHHA; values M and F converted to 1 and 2
SEXC	Gender of patient	Char 6	1.....Male	Recoded numeric

	labels		2.....Female	values from list provided by IHHA
ZIP	Zip code of patient's residence	Char 5	46241, etc.	IHHA
DIAGCAT	Diagnosis category	Num	10, 20, 30, 40, 50, 60, 70, 80, 88 See document "Proposed Methodology for Coding Asthma and Other Respiratory Disease" for classification criteria.	Derived from analysis criteria
DIAGCATC	Diagnosis category labels	Char 50	10.....Clearly asthma 20..... Possibly asthma 30.....Respiratory infections, upper tract 40.....Respiratory infections, middle and lower tract 50.....Noninfectious respiratory conditions, upper tract 60.....Noninfectious respiratory conditions, middle and lower tract 70..... Other diseases of the lung 80.....Respiratory symptoms 88.....Other	Derived from analysis criteria
DIAG3	Recoding of DIAGCAT	Char 25	10..... 1: Asthma 20.....2: Probably asthma Other.....3: Other respiratory 88..... 4: Other diagnosis	Derived from DIAGCAT
MEDHHINC	Median household income	Num	33724, etc.	CACI 99 DATA.XLS
PCTILE	Income percentile	Num	49, etc.	CACI 99 DATA.XLS
OSITEID	Ozone monitoring site ID	Char 16	18-095-0010, etc. (9 monitoring stations)	EPA AEROMETRIC INFORMATION RETRIEVAL SYSTEM (AIRS): Centroid of zip code area matched to closest monitoring site
OSITELOC	Ozone monitoring site location	Char 30	EAST ELEM. SCH., 893 E. US 36, PENDLETON, MADISON, etc.	AIRS
OZONMEAN	Ozone mean value for day	Num	0.024347685, etc.	Derived from hourly readings; missing if number of readings is less than 20
OZONEMAX	Ozone maximum value for day	Num	0.036, etc.	Derived from hourly readings
OZNMVAV2	Ozone 2-day moving average	Num	0.035499601, etc.	Derived from OZONMEAN
OZNMVAV3	Ozone 3-day moving average	Num	0.035499601, etc.	Derived from OZONMEAN
NOXMEAN	NOX mean value for day	Num	0.024347685, etc.	Derived from hourly readings; missing if number of readings is less than 20
NOXMAX	NOX maximum value for day	Num	0.036, etc.	Derived from hourly readings
NOXMVAV2	NOX 2-day moving average	Num	0.035499601, etc.	Derived from NOXMEAN
NOXMVAV3	NOX 3-day moving average	Num	0.035499601, etc.	Derived from NOXMEAN
SO2MEAN	SO2 mean value for day	Num	0.024347685, etc.	Derived from hourly readings; missing if number of readings is less than 20
SO2MAX	SO2 maximum value for day	Num	0.036, etc.	Derived from hourly readings

SO2MVAV2	SO2 2-day moving average	Num	0.035499601, etc.	Derived from SO2MEAN
SO2MVAV3	SO2 3-day moving average	Num	0.035499601, etc.	Derived from SO2MEAN
TEMPMAX	Air temperature maximum value for day	Num	56, etc.	Derived from hourly readings
TEMPMIN	Air temperature minimum value for day	Num	56, etc.	Derived from hourly readings
TEMPMEAN	Air temperature mean value for day	Num	56, etc.	Derived from hourly readings; missing if number of readings is less than 20
TMPMVAV2	Air temperature 2-day moving average	Num	58.5, etc.	Derived from TEMPMEAN
TMPMVAV3	Air temperature 3-day moving average	Num	61.3333333, etc.	Derived from TEMPMEAN
RLHMMAX	Relative humidity maximum value for day	Num	74, etc.	Derived from hourly readings
RLHMMIN	Relative humidity minimum value for day	Num	74, etc.	Derived from hourly readings
RLHMMEAN	Relative humidity mean value for day	Num	74, etc.	Derived from hourly readings; missing if number of readings is less than 20
RHMVAV2	Relative humidity 2-day moving average	Num	82.5, etc.	Derived from RLHMMEAN
RHMVAV3	Relative humidity 3-day moving average	Num	78.3333333, etc.	Derived from RLHMMEAN
DWPTMAX	Dew point maximum value for day	Num	35, etc.	Derived from hourly readings
DWPTMIN	Dew point minimum value for day	Num	35, etc.	Derived from hourly readings
DWPTMEAN	Dew point mean value for day	Num	35, etc.	Derived from hourly readings; missing if number of readings is less than 20
DPMVAV2	Dew point 2-day moving average	Num	41.5, etc.	Derived from DWPTMEAN
DPMVAV3	Dew point 3-day moving average	Num	42.3333333, etc.	Derived from DWPTMEAN
TOTPOL	Total pollen count for the day	Num	45, etc.	24-hr averages provided by Dr. Frank Wu & Harvard School of Public Health
POLMVAV2	Pollen 2-day moving average	Num	12.5, etc.	Derived from TOTPOL
POLMVAV3	Pollen 3-day moving average	Num	23.3333333, etc.	Derived from TOTPOL
TOTSPO	Total spore count for the day	Num	1245, etc.	24-hr averages provided by Dr. Frank Wu & Harvard School of Public Health
SPOMVAV2	Spore 2-day moving average	Num	512.5, etc.	Derived from TOTSPO
SPOMVAV3	Spore 3-day moving average	Num	723.3333333, etc.	Derived from TOTSPO
PM10MEAN	Mean PM10 count for six-day period	Num	41.293847582, etc.	Derived from readings taken every six days
PBMEAN	Mean PB count for six-day period	Num	0.034857493, etc.	Derived from readings taken every six days
OZMEANDC	Decile recoding of OZONMEAN	Num	0.0365, etc.	Derived from OZONMEAN using PROC UNIVARIATE

OZMAXDC	Decile recoding of OZONEMAX	Num	0.0215, etc.	Derived from OZONEMAX using PROC UNIVARIATE
OZMV2DC	Decile recoding of OZNMVAV2	Num	0.016, etc.	Derived from OZNMVAV2 using PROC UNIVARIATE
OZMV3DC	Decile recoding of OZNMVAV3	Num	0.027, etc.	Derived from OZNMVAV3 using PROC UNIVARIATE
NXMEANDC	Decile recoding of NOXMEAN	Num	0.013, etc.	Derived from NOXMEAN using PROC UNIVARIATE
NXMAXDC	Decile recoding of NOXMAX	Num	0.0395, etc.	Derived from NOXMAX using PROC UNIVARIATE
NXMV2DC	Decile recoding of NOXMVAV2	Num	0.015, etc.	Derived from NOXMVAV2 using PROC UNIVARIATE
NXMV3DC	Decile recoding of NOXMVAV3	Num	0.018, etc.	Derived from NOXMVAV3 using PROC UNIVARIATE
S2MEANDC	Decile recoding of SO2MEAN	Num	0.0015, etc.	Derived from SO2MEAN using PROC UNIVARIATE
S2MAXDC	Decile recoding of SO2MAX	Num	0.009, etc.	Derived from SO2MAX using PROC UNIVARIATE
S2MV2DC	Decile recoding of SO2MVAV2	Num	0.0035, etc.	Derived from SO2MVAV2 using PROC UNIVARIATE
S2MV3DC	Decile recoding of SO2MVAV3	Num	0.007, etc.	Derived from SO2MVAV3 using PROC UNIVARIATE
PMMEANDC	Decile recoding of PM10MEAN	Num	11.155, etc.	Derived from PM10MEAN using PROC UNIVARIATE
TPMEANDC	Decile recoding of TEMPMEAN	Num	53.157, etc.	Derived from TEMPMEAN using PROC UNIVARIATE
TPMAXDC	Decile recoding of TEMPMAX	Num	60.5, etc.	Derived from TEMPMAX using PROC UNIVARIATE
TPMINDC	Decile recoding of TEMPMIN	Num	40.5, etc.	Derived from TEMPMIN using PROC UNIVARIATE
TPMV2DC	Decile recoding of TMPMVAV2	Num	53.9115, etc.	Derived from TMPMVAV2 using PROC UNIVARIATE
TPMV3DC	Decile recoding of TMPMVAV3	Num	55.51, etc.	Derived from TMPMVAV3 using PROC UNIVARIATE
RHMEANDC	Decile recoding of RLHMMEAN	Num	66.7825, etc.	Derived from RLHMMEAN using PROC UNIVARIATE
RHMAXDC	Decile recoding of RLHMMAX	Num	95, etc.	Derived from RLHMMAX using PROC UNIVARIATE
RHMINDC	Decile recoding of RLHMMIN	Num	57.5, etc.	Derived from RLHMMIN using PROC UNIVARIATE
RHMV2DC	Decile recoding of RHMMVAV2	Num	64.2825, etc.	Derived from RHMMVAV2 using PROC UNIVARIATE
RHMV3DC	Decile recoding of	Num	60.0755, etc.	Derived from

	RHMMVAV3			RHMMVAV3 using PROC UNIVARIATE
DPMEANDC	Decile recoding of DWPTMEAN	Num	36.7615, etc.	Derived from DWPTMEAN using PROC UNIVARIATE
DPMAXDC	Decile recoding of DWPTMAX	Num	57.5, etc.	Derived from DWPTMAX using PROC UNIVARIATE
DPMINDC	Decile recoding of DWPTMIN	Num	29.5, etc.	Derived from DWPTMIN using PROC UNIVARIATE
DPMV2DC	Decile recoding of DPMVAV2	Num	37.9845, etc.	Derived from DPMVAV2 using PROC UNIVARIATE
DPMV3DC	Decile recoding of DPMVAV3	Num	39.8395, etc.	Derived from DPMVAV3 using PROC UNIVARIATE
OZ9HMEAN	Ozone mean value for 9 hours, 10am-6pm	Num	0.029, etc.	Derived from hourly readings; missing if number of readings is less than 5
OZ9HMAX	Ozone maximum value for 9 hours, 10am-6pm	Num	0.038, etc.	Derived from hourly readings
OZ9MVAV2	Ozone 2-day moving average, 9 hours, 10am-6pm	Num	0.044, etc.	Derived from OZ9HMEAN
OZ9MVAV3	Ozone 3-day moving average, 9 hours, 10am-6pm	Num	0.049, etc.	Derived from OZ9HMEAN
OZ9HMNDC	Decile recoding of OZ9HMEAN	Num	0.021, etc.	Derived from OZ9HMEAN using PROC UNIVARIATE
OZ9HMXDC	Decile recoding of OZ9HMAX	Num	0.0275, etc.	Derived from OZ9HMAX using PROC UNIVARIATE
OZ9MV2DC	Decile recoding of OZ9MVAV2	Num	0.0445, etc.	Derived from OZ9MVAV2 using PROC UNIVARIATE
OZ9MV3DC	Decile recoding of OZ9MVAV3	Num	0.0505, etc.	Derived from OZ9MVAV3 using PROC UNIVARIATE